THE ROLE OF HYPERTONIC SOLUTIONS IN RESUSCITATION OF HAEMORRHAGIC SHOCK IN EXPERIMENTAL ANIMALS

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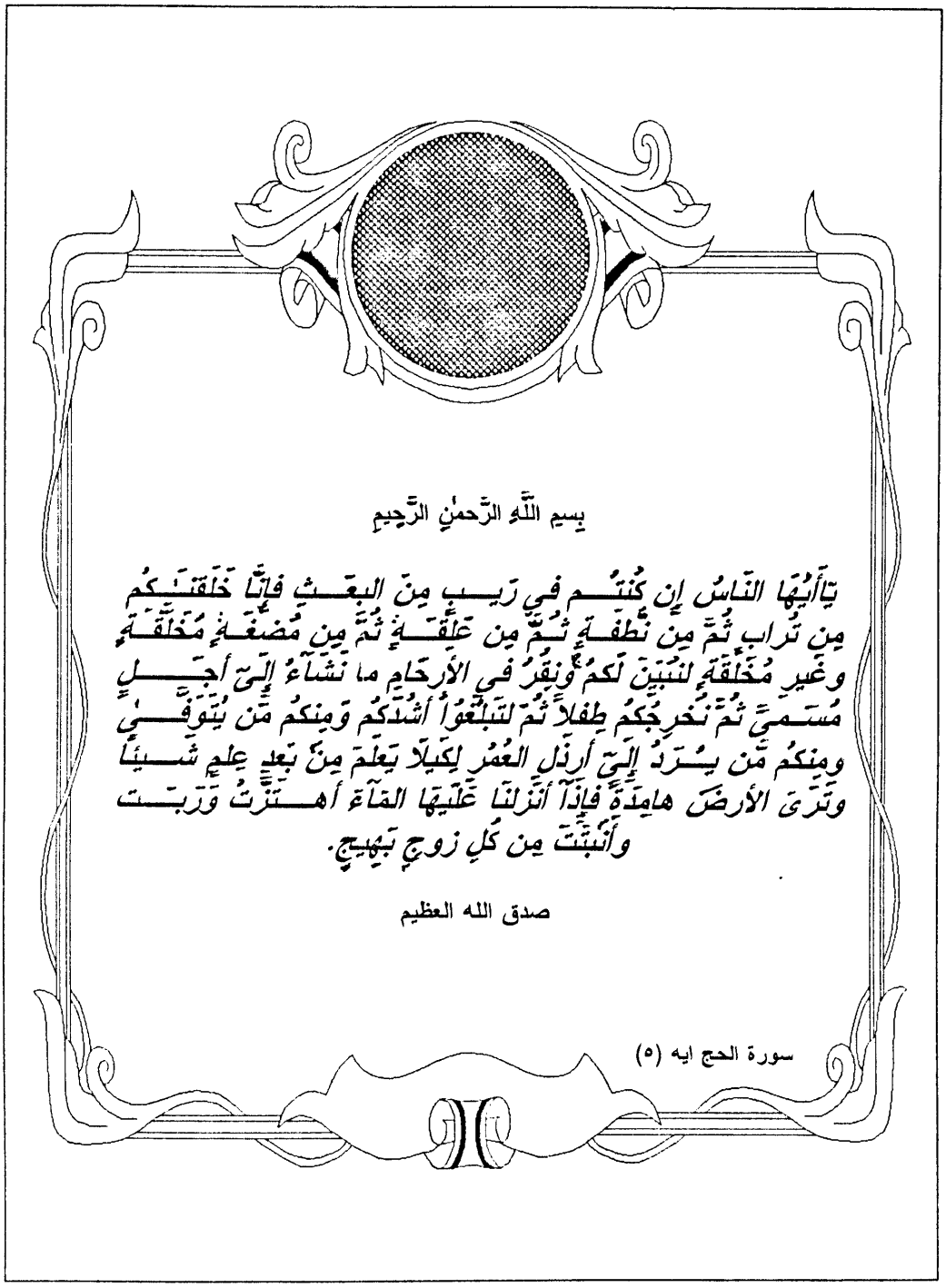

بِسمِ اللَّهِ الرَّحمٰنِ الرَّحِيمِ

يَاأَيُّهَا النَّاسُ إِن كُنتُمْ فِي رَيْبٍ مِنَ الْبَعْثِ فَإِنَّا خَلَقْنَاكُم مِن تُرَابٍ ثُمَّ مِن نُّطْفَةٍ ثُمَّ مِن عَلَقَةٍ ثُمَّ مِن مُّضْغَةٍ مُّخَلَّقَةٍ وَغَيْرِ مُخَلَّقَةٍ لِّنُبَيِّنَ لَكُمْ وَنُقِرُّ فِي الْأَرْحَامِ مَا نَشَاءُ إِلَىٰ أَجَلٍ مُّسَمًّى ثُمَّ نُخْرِجُكُمْ طِفْلًا ثُمَّ لِتَبْلُغُوا أَشُدَّكُمْ وَمِنكُم مَّن يُتَوَفَّىٰ وَمِنكُم مَّن يُرَدُّ إِلَىٰ أَرْذَلِ الْعُمُرِ لِكَيْلَا يَعْلَمَ مِن بَعْدِ عِلْمٍ شَيْئًا وَتَرَى الْأَرْضَ هَامِدَةً فَإِذَا أَنزَلْنَا عَلَيْهَا الْمَاءَ اهْتَزَّتْ وَرَبَتْ وَأَنبَتَتْ مِن كُلِّ زَوْجٍ بَهِيجٍ.

صدق الله العظيم

سورة الحج ايه (٥)

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*First and foremost, thanks to **ALLAH**,*

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INTRODUCTION AND AIM OF THE WORK

INTRODUCTION

Despite the advances in primary care, trauma in conjunction with shock remains the leading cause of morbidity and mortality in teenagers and young adults **(Kreimeier et al., 1993).**

It has become an established fact that the primary factor rendering patients at risk of developing multiple system organ failure (MSOF) and late deaths after trauma shock and is the persistence of impaired microcirculation, with tissue hypoxia and deterioration of cellular function **(Bihardi, 1989).**

Prehospital, preoperative and intensive care related efforts aim to reduce the number of trauma deaths through the improvement of resuscitation from hypovolemia and systemic hypotension and the rapid restoration of oxygen delivery to the tissues **(Fleming et al., 1992).**

The systematic experimental studies concerning hyperosomatic solutions began in 1960's; however the use of hyperosomotic solutions for the initial therapy of hypovolemic shock began in 1980's **(Kreimeir and Messmer, 1988).**

The term "small-volume resuscitation" was first coined by **Nakayama (1984)**, who showed, in a sheep model of hypovolemic shock, that cardiac output was restored and systemic pressure significantly increased immediately after the infusion of hyperosmotic saline 7.5% NaCl = 2400 mosmol/liter, even when the volume supplied was as small as 10% of the total blood loss **(Nakayama et al., 1984).**

During recent years, many experimental and several clinical studies have been performed that have investigated the efficacy of different hyperosmotic solutions (NaCl, 7.5%, glucose, mannitol, $NaHCo_3$, sodium acetate, lactated saline), volume range (4 - 6 ml/Kg), duration of injection (over 2 - 15 min) and route of administration (intravenous/intraosseous), with respect to restoration of macro-and microcirculatory parameters, organ function and ultimately survival **(Kreimeier et al., 1993).**

AIM OF THE WORK

The present work was designed to investigate the role of different hypertonic solutions in resuscitation of experimentally induced controlled haemorrhagic shock in albino rats.

REVIEW OF LITERATURE

PATHOPHYSIOLOGY OF HAEMORRHAGIC SHOCK

Trauma often includes considerable losses of blood and plasma that may lead to hypovolaemia and shock. The initial response of the body to trauma and haemorrhage is characterized by a neuroendocrine-mediated general defence reaction for the maintenance of circulatory hemostasis and substrate availability for vital organ function. Endogenous fluid is mobilized from intracellular and interstitial sources into the vascular compartment. This transcapillary refill is achieved by activation of glucose, osmotic and neurogenic adaptive vascular mechanisms. The metabolic consequences of insufficient tissue perfusion are anaerobic glycolysis with increased production of lactate and hydrogen ions, acidosis, impaired mitochondrial energy production, disturbed ionic homeostasis across cell membranes, and reduced functional capacity of

tissue cells (**Mouchawar and Rosenthal, 1993**). The shock and trauma induced alterations in tissue perfusion and metabolism vary, depending on the auto regulatory capacity of an organ, its basal metabolic requirements, its high energy phosphagen reserves, and its ongoing functional activity.

Metabolic alterations impairing organ function occur early in the kidney and the liver and late in the heart and the brain (**Haliamac, 1993**).

The ischemic tolerance of the skeletal muscle cell is considerable but vast amounts of lactic acid are produced, which at reperfusion will reach central blood and disturb vital organ function. Tissue factors released from mechanically traumatized or hypoxic cells will activate cascade systems and may induce alterations in remote organs, resulting in the development of multiorgan failure (**Mouchawar and Rosenthal, 1993**).

However, shock is defined as a clinical syndrome characterized by protracted prostration, pallor, coldness and moistness of the skin, collapse of the superficial veins, alteration in the mental status, and suppression of the formation of urine. The systolic arterial pressure is usually less

than 90 mmHg or has declined more than 50 mmHg from the basal level and the urine flow is less than 20 ml/hour. The urine is typically iso-osmolar. The ratio between urine osmolality and plasma osmolality, which reflects the tubular concentrating function of the nephron, is characteristically less than 1.5 **(Weil et al., 1979).**

The basic mechanism underlying all forms of acute circulatory shock is reduction of effective blood flow and inadequate tissue perfusion with decreased delivery of oxygen to the capillary exchange bed **(Weil et al., 1972).**

The clinical signs of shock reflect primary perfusion failure. Reduction in peripheral blood flow accounts for cold, cyanotic extremities, reduction in cerebral blood flow for altered mental alertness, reduction in renal perfusion for changes in the quantity and quality of urine excreted, and reduction in coronary blood flow for compromised myocardial oxygen supply and electro cardiographic S-T segment and T-wave changes which are indicative of myocardial ischemia **(Weil et al., 1979).**

With reduction in tissue perfusion and decreased delivery of oxygen to the capillary exchange bed, oxidative metabolism is impaired,

there is decreased formation of high energy phosphate bonds and an increase in the permeability of cellular membranes. The cellular sodium pump fails and sodium enters and potassium escapes from the cells. The cells swell and ultimately there is rupture of lysosomal membranes with release of lytic enzymes and autodigestion **(Weil et al., 1967).**

In the absence of metabolic oxygen, the anaerobic pyruvate-lactate shunt is activated and this accounts for the production of excesses of lactic acid and intracellular acidosis. The magnitude of lactic acidosis corresponds to the severity of the oxygen deficit **(Shubin et al., 1974).**

At the start of haemorrhagic shock the pre-and post-capillary sphincters are tightly constricted allowing little blood to enter the capillary bed. The pre-capillary sphincter then loses tone due to local anoxia and the accumulation of acid metabolites, while the post-capillary sphincter remains constricted. This leads to capillary engorgement and stagnation, with extravasation of fluid causing further depletion of the blood volume. Ultimately there is capillary destruction and loss of frank blood. The onset of this state during prolonged haemorrhagic shock marks the change of the condition from reversible to irreversible, in other words the point at which restoration of blood volume alone is insufficient to prevent progressive deterioration and death **(Wyilie and Davidson, 1978)**.

A valuable update on haemodynamic and neurohumoral responses to acute hypovolemia is available, the course of sympathetic and other humoral responses is divided into sympathoexicitatory and sympathoinhibitory phases. During the former, arterial pressure is maintained at the expense of sympathetic and renin mediated selective vasoconstriction. The sympathoinhibitory phase develops abruptly, after a blood loss of approximately 30%, and is signaled by bradycardia and a profound fall in arterial pressure **(Rocha et al., 1992).**

A large number of central and peripheral neurotransmiters are known or thought to be involved in the neural pathways that make up the integrated response to acute hemorrhage. Opioid peptides have been implicated with acute blood loss. Recently it has been shown that the release of vasopressin induced by hypotensive haemorrhage is inhibited by opioid peptides, but the relevance of this interaction with regard to the haemodynamics of shock is controversal **(Schadt and Hasser, 1991).** However, the intracerebroventricular administration of morphine has been shown to inhibit long-term survival response produced by small-volume hypertonic resuscitation in dogs **(Velasco et al., 1990).**

Central and peripheral serotonergic pathways have also been implicated with the hypotensive phase of acute blood loss. It was

suggested that its main role was attributed to the activation of the sympatho-inhibitory phase of hypotensive haemorrhage **(Evans et al., 1990).**

Cholinesterase inhibitors, such as physostigmine may also play a role in the correction of hypotensive hemorrhage. Its effect appears to be mainly a result of an alteration of the pre-capillary : Post-capillary resistance ratio, which would shift the capillary exchange balance further towards reabsorption of fluid. The probable mechanism involves the general sympathetic activation induced by these agents **(Savic et al., 1991).**

The renin-angiotensin system plays a well-established major role in the complex response to acute blood loss, but apparently it is not responsible for the severe restriction of hepatic blood flow observed after blood loss, as shown by the fact that pentoxifyllin, a methyl-xanthine phosphodiesterase inhibitor, improves hepatic blood flow after resuscitation from shock whereas saralasin, the angiotensin-converting enzyme inhibitor, is without action **(Flynn et al., 1991).** On the other hand, central angiotensinergic mechanism appears to be essential for the stable haemodynamic recovery from haemorrhage produced by hypertonic NaCl **(Velasco et al., 1990).**

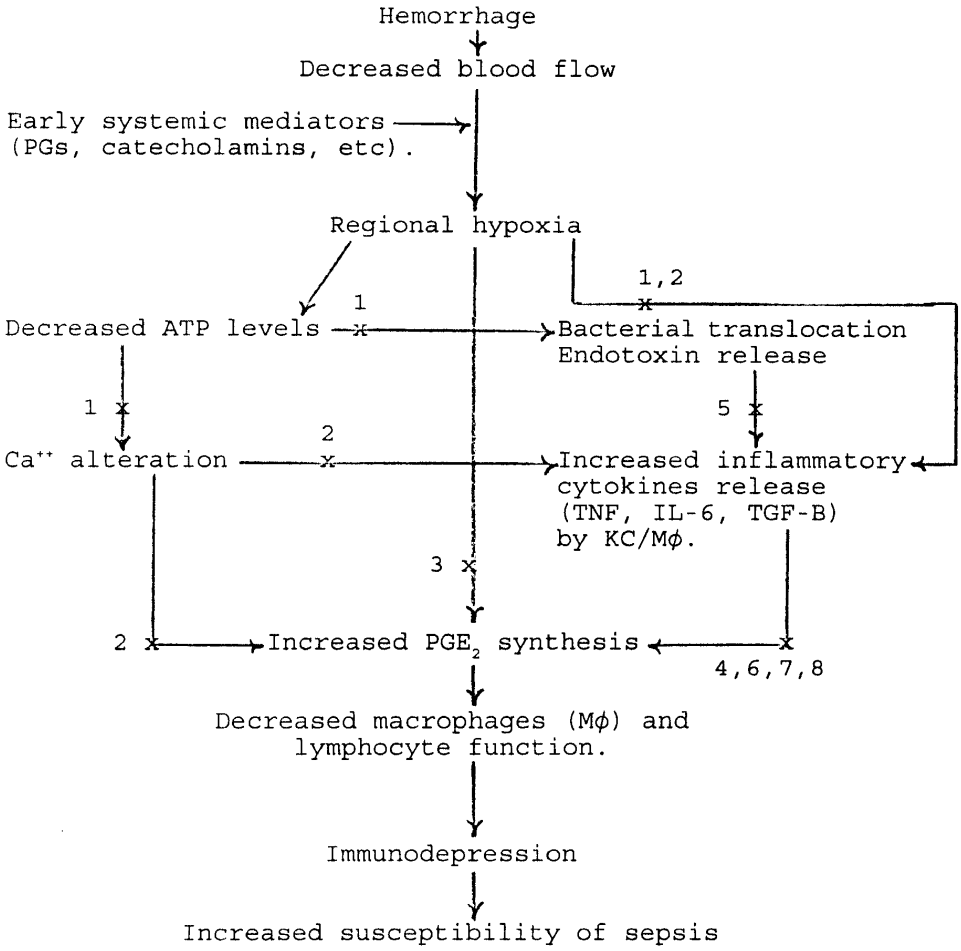
It has been also found that, the cerebral production of thromboxan A_2 appears to be enhanced by the combination of haemorrhage and increased intracranial pressure **(Kong et al., 1991)** whereas splanchnic prostacyclin synthesis is decreased by prolonged haemorrhage **(Myers and Small, 1991).**

Haemoglobin affinity for oxygen may be a critical factor in the evolution of severe and prolonged shock. It has been shown that acid-base parameters and long-term survival are considerably improved when the Po_2 at 50% of oxyhaemoglobin saturation (P50) is raised **(Bercovich et al., 1991).** This may be caused by the fact that a right shift of the Bohr affinity curve will not affect the uptake of oxygen in the lung, but may considerably increase its down load at tissue level and thereby increase oxygen uptake "Vo2" for any given oxygen supply "Do2" **(Rocha et al., 1992).**

A hypothesis of the cascade of events following hemorrhagic shock that leads to immuno-suppression and increased susceptibility to sepsis has been proposed **(Chaudry and Ayala, 1993)**, as haemorrhage causes decreased blood flow, which produces regional hypoxia, leading to decreased cellular ATP levels and increases inflammatory cytokine release and PGE_2 synthesis. Moreover, regional hypoxia may cause

bacterial translocation/endotoxin release which can also cause increased inflammatory cytokine release. The decreased cellular ATP levels cause alterations in intracellular calcium homostasis, thereby altering the immune cell's second messenger system. Thus, regional hypoxia directly and indirectly, via decreased ATP levels, calcium alterations, and increased inflammatory cytokine release, leads to increased PGE_2 synthesis. This results in depression in macrophage and lymphocyte functions, immunodepression, and increased susceptibility to infection. **(Chaudry and Ayala, 1993)**.

In this hypothesis a variety of potential steps have been proposed at which the cascade of events could be interrupted to lock the deleterious consequences of hemorrhage (Fig. 1 by **Chaudry and Ayala, 1993**). The experimental use of agents such as ATP-$MgCl_2$ and TNF antibodies, ibuprofen, chloroquine or cyclooxygenase inhibitors to interrupt the haemorrhage induced cascade of events not only restores the depressed immunological responses but also prevents the increased lethality from sepsis following haemorrhage **(Chaudry and Ayala, 1993)**.



* *Cascade inhibitors.*	* *Antibodies against:*
1. ATP-$MgCl_2$.	5. LPS.
2. Ca^{++} antagonists.	6. TNF
3. Cyclo-oxygenase inhibitors.	7. IL-6.
4. Chloroquine.	8. TGF.B.

Abbreviations :

LPS = Lipopolysaccharide TNF = Tumour necrosis factor
IL-6 = Interleukin 6
TGF-ß = Transforming growth factor-ß

Fig. (1) : Cascade of events following haemorrhage leading to immunodepression **(Chaudry and Ayala, 1993).**

OXYGEN TRANSPORT AND HAEMORRHAGIC SHOCK

The primary role of the circulation is to continuously provide oxygen at levels adequate for tissue oxygen requirements. There is accumulating evidence that shock is a substantially more subtle phenomenon than it was previously judged to be. Clinical assessment and resuscitation of the circulation has been based upon blood pressure and flow for over a century, However, it is apparent that blood pressure, and even cardiac output fails to adequately describe circulatory abnormalities in all circumstances. By assessing the relationship of oxygen consumption (uptake) VO_2 to oxygen delivery DO_2 it may be possible to determine if resuscitation is adequate or inadequate **(Lawrence, 1993)**.

At lower levels of Do_2, Vo_2 appears to be directly dependent upon the levels of Do_2 this is termed the "supply dependent" phase of the relationship. At higher levels of Do_2, Vo_2 is independent of Do_2, this is termed the "supply independent" phase. The point of change between these two phases has been termed the "anaerobic" threshold or critical level Do_2 "Do_2 crit" **(Lawrence, 1993)**.

To best improve Do_2, it remains controversial whether cardiac output should be enhanced by volume infusion or inotropic drugs, or haemoglobin increased by blood transfusion. A recent study by **Ward et al. (1992)** created condition of high blood flow-low O_2 or of low blood flow-high O_2, and measured diaphragmatic muscle tension generation. Despite equivalent Do_2, diaphragmatic muscle functions better when perfusion is maintained rather than when blood haemoglobin concentration is maintained. One explanation may be that inadequate perfusion allows the closure of microvessels, so that even if the deficit in bulk Do_2 is compensated for by an adequate haemoglobin concentration, less tissues is perfused and function is impaired.

However, previous studies have suggested that survivors of critical illness in general had higher than normal levels of cardiac output, oxygen delivery and oxygen uptake. Whereas those patients who failed to survive had only normal levels of these variables. Therefore, it has been considered a potential therapeutic manoeuver to increase oxygen delivery by increasing cardiac output in an attempt to insure a "supply independent" state and thereby produce a condition more likely to result in patient survival (**Rashkin et al., 1985**).

MONITORING OF HYPOVOLEMIA

Hypovolemia still remains a diagnostic challenge for the anaesthesiologist and critical care physician. Conventional haemodynamic parameters, such as blood pressure, heart rate, and even central venous pressure (CVP) and pulmonary capillary wedge pressure (PCWP), have been shown repeatedly to be insensitive and misleading in the assessment of effective blood volume (**Messinger et al., 1993**). One reason for the inadequate ability of the clinical response to reflect the degree of haemorrhage is the differential distribution of blood flow in patients with acute blood loss. It has been found that the distribution of blood flow to some organs as the skin and pancreas, decrease with even small losses of blood volume. On the other hand, the kidney maintains normal blood flow with blood losses of up to 40%, and become very sensitive to any further lowering of blood volume (**Gosain et al., 1991**).

Blood pressure :

The most commonly used parameter for diagnosing hypovolemia is the blood pressure (BP). An early sign of haemorrhage is the reduction of pulse pressure, which is initially a result of an increase in the diastolic BP caused by vascular constriction. The decrease in systolic BP appears

later following a greater reduction in the blood volume (**Davis et al., 1992**).

In situations of stress, such as during apprehension following trauma, the increased secretion of endogenous catecholamines may delay the reduction in BP despite a reduction in blood volume. on the other hand, during anaesthesia, the effects of anaesthetic agents may cause a reduction in BP even if blood volume is normal. Thus the blood pressure measurement is an inaccurate tool, with a low specificity and sensitivity for the diagnosis of hypovolemia. In order to improve the accuracy of BP measurement in the diagnosis of hypovolemia, the positional changes in blood pressure may be measured (**Messinger et al., 1993**). However, **Baraff and Schringer (1992)** had studied the orthostatic changes in pulse and blood pressure in blood donors after blood loss of about 450 ml. They found that the sensitivity and specificity of the orthostatic changes in heart rate and blood pressure were quite poor. Thus, the use of orthostatic changes of vital signs to detect subtle hypovolemia is not clinically useful.

Pulse rate :

Tachycardia which classically accompanies the development of acute hypovolemia may not appear when hypovolemia occurs during

anaesthesia, because, baroreflex activity is decreased by anaesthetic agents. On the other hand, many other factors beside hypovolemia may cause tachycardia. Thus, tachycardia is neither sensitive nor specific for the detection of hypovolemia (**Messinger et al., 1993**).

Central venous pressure :

The central venous pressure (CVP) is commonly utilized as a parameter of volume status. The CVP is a measure of the right atrial pressure (P_{ra}), which is supposed to reflect right atrial volume. However, using CVP as a parameter of volume can be misleading because the CVP is influenced by other factors such as intrathoracic pressure, arrhythmias and pulmonary hypertension. Also, the interpretation of the CVP may be problematic in patients who are on positive pressure ventilation, particulary with high levels of positive-end expiratory pressure (**Mark, 1991**).

Moreover, the measurement of the right sided pressure (CVP) may not reflect the filling status of the left heart (left ventricular end diastolic pressure) particulary in patients with increased right ventricular afterload, which is common in patients with chronic obstructive lung disease and corpulmonale. However, a significant increase (3 - 5 cm H_2O) in CVP, in response to 200 ml of crystalloid solution administered over 10 - 15

min, will indicate that the blood volume of the patient is relatively adequate, as opposed to a situation in which the CVP is unaffected by such fluid challenge (**Messinger, 1993**).

The pulmonary capillary wedge pressure :

The assessment of the left ventricular preload may be obtained by using the pulmonary artery catheter (PAC). Measurement of the pulmonary capillary wedge pressure (PCWP) provides an indication of the left ventricular end diastolic volume by estimating the LVEDP. The ability of the PCWP to reflect LVEDP depends on the continuity of the fluid column from the catheter tip to the left ventricle. In situations such as mitral stenosis, tachycardia, and positive pressure ventilation the PCWP may not reflect the LVEDP. However, Despite these limitations, the PAC has been shown to be useful in improving therapy in up to 50% of patients in the intensive care unit (**Steingruph et al., 1991**).

Another option that was recently added to the PAC is a rapid response thermistor which enables the calculation of the right ventricular volume and ejection fraction. This technique has been described as a more accurate means of assessing volume and cardiac function than the PCWP determinations alone (**Dennis et al., 1991**).

Echocardiography :

The cardiogram both transthoracic and traneosophageal can provide rapid noninvasive information about heart volumes and function, and can differentiate between hypovolemia or a poorly functioning heart as a cause of circulatory failure. There is no doubt that, measurement of left ventricular end diastolic area by ecocardiography provides the most accurate assessment of the preload of the ventricle, as it has been shown by **Clements et al, (1988)**, that the correlation of LVED area with LVED volume, as measured by first pass radionucleotide angiography is excellent.

Arterial pressure waveform analysis :

A new modality for assessing volume status in patients who are being mechanically ventilated with positive pressure ventilation is that of pressure waveform analysis. The arterial pressure waveform demonstrates a typical biphasic change with each mechanical breath. The initial response is an increase in the systolic BP, which is caused mainly by a squeezing effect of the inflating lung on the pulmonary vasculature, leading to transient increase in the LV preload. The initial increase in the systolic BP is followed by a decrease, which is caused by a lower LV stroke output attributed to the reduction in venous return that is associated with the mechanical breath. The difference between the maximal and minimal values of the systolic BP during one mechanical

beath is termed the systolic pressure variation by using the systolic BP during a short (5 seconds) apnea as a reference pressure, the systolic pressure variation (delta) can be divided into "d up" and "d Down" components (Fig. 2). The "d up" reflects the augmentation of the LV stroke output by the mechanical breath, whereas the "d Down" reflects the extent by which the reduction in venous return affects the LV stroke output. Patients with a reduced preload are more susceptible to the reduction in venous return with every breath, and therefore demonstrate a large "d Down" of more than 10%. On the other hand, congestive heart failure, is characterized by a near total disappearance of the "d Down" while the "d up" becomes the most prominent respiratory induced variation in the Bp waveform. Thus, the systolic pressure variation is extremely helpful in differentiating hypovolemia from heart failure as the cause of a low-flow state **(Messinger et al., 1993)**.

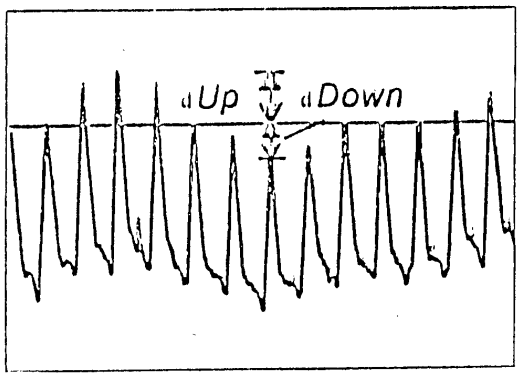


Fig. (2) : *The systolic pressure variation is the difference between the maximal and minimal values of the systolic blood pressure during one cycle of a mechanical breath* ***(Messinger et al., 1993)***.

Arterial pressure waveform analysis requires fixation of an arterial line, however, the same information can be obtained from observing the plethesmographic signal of the pulse oximeter. The waveform of the oximeter responsds to the cyclic changes in the intrathoracic pressure, and in hypovolemia there is a large variability in the amplitude of the signal with every breath **(Messinger et al., 1993).**

The main advantage of this approach to volume assessment is that it requires very little in terms of equipments, in the critically ill patient who is often on mechanical ventilation A "d Down" in excess of 10% of the systolic Bp during apnea is highly suggestive of hypovolemia **(Messinger et al., 1993)**.

Indicators of poor tissue perfusion :

An alternative approach to haemodynamic monitoring for the detection of hypovolemia is the measurement of biochemical parameters that appear during low tissue perfusion states like-subcutaneous Po_2, arterial or mixed venous lactate or PH, and arterial-venous PCo_2 difference **(Messinger et al., 1993)**.

FLUID THERAPY

Fluid therapy is the treatment of hypovolemia but the appropriate solution and infusion regimen is often controversial. However, the ideal goal of resuscitation from severe haemorrhagic shock is the restoration of cardiac output (CO) and its adequate distribution to all organs and tissues, as this ensures sufficient oxygen supply (DO_2) and adequate oxygen uptake (VO_2). So, resuscitation regimens which maximize DO_2 without excessive extravascular sequestration of fluid should be a goal of future research **(Kramer and Wallfisch, 1992).**

Fluids used for resuscitation :

1. **Crystalloids :**

Glucose solutions essentially provide free water because glucose is metabolized rapidly. As the total body water represents about 60% of body weight and plasma volume about 4%, less than 10% of an administered solution of glucose remains in the vascular space. Therefore, glucose solutions are ineffective plasma expanders **(Vincent, 1991).**

Saline solutions are distributed into the extracellular space, which represents about 33% of total body water. Thus

approximately 25% of the normal saline infused remains in the vascular space. The administration of normal saline may result in hypernatraemia and hyperchloraemic acidosis. **Therefore, Ringer's lactate** solution, which has a slightly smaller sodium content but which contains lactate (metabolized to bicarbonate), is often preferred when massive crystalloid infusions are administered **(Vincent, 1991).**

2. Colloids :

Colloids increase plasma oncotic pressure and so draw fluid into the intravascular space. This group includes dextran, gelatins and albumin.

Natural colloids include 5% and 25% albumin solutions. The 5% solution remains largely within the vascular space when the capillary membrane is intact so that it represents a natural plasma expander. The hyperoncotic 25% solution pulls fluid from the interstitial space, so that it may be preferred in oedematous patients **(Vincent, 1991).**

Synthetic colloids include dextran, starch and gelatins. Dextran is available as dextran 70 and dextran 40. Dextran 70 is non-toxic, electrically neutral, and chemically inert. It has an acid pH and may

degrade acid-labile drugs. Although it is eventually eliminated completely from the body, 25% is excreted within 3 h, it remains in the circulation in gradually decreasing amount up to a week. It has proved useful as a plasma substitute in cases of burns and surgical shock and also in prophylaxis of shock during operations. It increases the venous return to the heart. Dextran 70 is the most widely used plasma expander and 500 ml will usually increase the circulating plasma volume by 750 ml. Also it is effective in prevention of venous thrombo-embolism **(Atkinson, 1987).**

Hetastarch (hydroxyethyl starch) is available as a 6% solution with an average molecular weight of 450,000. It is highly effective as a plasma expander and less expensive than albumin. Coagulation studies and bleeding times are generally not significantly affected after infusion of 1-2 liters. Hetastarch is non antigenic, and anaphylactoid reactions are rare **(Edward and Maged, 1992).**

3. Hypertonic solutions :

In experimental studies of traumatic shock hypertonic solutions have been shown to be superior to normotonic solutions in terms of restoration of arterial pressure, diuresis, cardiac output, oxygen transport and oxygen consumption, and ultimate survival **(Stanford et al., 1989).**

In addition to the larger volume effect, other factors can contribute to the better haemodynamic effects of hypertonic solutions. The effect of hyperosmolarity and hypernatraemia on myocardial contractility are complex and still controversial as myocardial contractility has been found sometimes to increase and sometimes to decrease, these may be explained by differences in the type and degree of hyperosmolarity and also the model used, however a sympathetic response can compensate for intrinsic myocardial depression **(Wildenthal, 1969).**

Hypertonic solutions may also increase the myocardial availability of calcium, cardiac function may also be improved by the direct vasodilating effects of hyperosmolar solutions, a reflex vagal mechanism may also play a role **(Lopes et al., 1981).**

Characteristics of hypertonic NaCl solutions (7.5%) include an osmolarity of 2400 mos/liter, a sodium content of 1200 mEq/liter, a molar concentration of 1.2 M and an osmotic pressure of 45600 mmHg **(Treutz and Friedl, 1992).** The beneficial effect of this solution, however is restricted to approximately 15 - 20 min. The addition of 6% dextran 70 to this solution prolongs its effect to approximately 45 min and recent studies seem to indicate that this hypertonic hyperoncotic solution is superior to lactated Reinger's solution or other crystalloids for trauma victims in military or civilian settings **(Mattox et al., 1991).**

Hypertonic solutions and haemorrhagic shock :

The efficacy of hypertonic solutions in improving the haemodynamic status has been shown in various experimental models, and recent clinical studies have suggested that hypertonic saline solutions may be beneficial during resuscitation of the injured patient (**Trentz and Friedl, 1992**). In the prehospital and emergency room setting hypertonic saline 7.5% is currently favoured, as 7.5% NaCl allows rapid improvement of the haemodynamic state with rapidly given small volumes (4 - 5 ml/kg) of fluid (**Mattox et al., 1991).**

The effect of hypertonic solutions on global organ perfusion have been studied by **Kreimeier et al. (1990)**, in a comparative study between the effect of hypertonic saline-dextran (HSD) versus hypertonic saline and hyperoncotic dextran using a canine model of severe haemorrhagic hypotension. Besides macro-haemodynamics, the fractional distribution of cardiac output and organ blood flow in the kidney, pancreas, gastric mucosa, small intestine, colon, myocardium, brain, skeletal muscle and adrenal glands were measured. According to their results, small volume (4 ml/kg) application of 7.2% saline / 10% dextran 60 (HSD) provides instantaneous restitution of regional organ blood flow and apparently a more uniform circulatory response can be achieved as compared with 7.2% saline or 10% dextran 60 alone.

Behrman et al. (1991) compared macroscopic and microscopic distributions of blood flow in swine during haemorrhage and resuscitation with an initial infusion of either hypertonic saline/dextran (HSD) or Ringer's lactate (RL). Follow-up infusion of RL was performed to maintain arterial pressure at base line. Despite equal macroscopic blood flows in the superior mesenteric artery and abdominal aorta, microcirculatory perfusion was higher in the jejunal mucosa and renal cortex of HSD treated animals.

Pascual et al. (1992) used isotonic LR and HSD to normalize aortic blood flow after intraoperative hypovolemia in pigs. Pulmonary vascular pressure, atrial filling pressure and cardiac work were greater after isotonic therapy compared with hypertonic resuscitation. These data suggest that hypertonic formulations may offer real physiological benefit in the operating room and that their use may extend beyond prehospital emergency room use.

A trial on HSD for resuscitation of trauma patients undergoing helicopter transport shows that HSD caused a significant improvement in arterial blood pressure on arrival at hospital, and a borderline improvement of 7-day survival in the subpopulation with severe head injury. In addition, there was a reduction in arterial pressure during

transport in a smaller number of HSD treated patients (10 out of 83) as compared with the standard treatment group (19 out of 83). However HSD did not induce a higher blood requirement within the first 24 h in hospital (**Vasser et al., 1991**).

Hypertonic solutions and septic shock :

It has been recently well established that resuscitation of shock and ischemia to normal global flows does not preclude hidden ischaemia in some organs, in particular, the gut has sustained reduction in blood flow despite cardiac indices above normal (**Scalla et al., 1990**). The clinical relevance of gut ischemia may be profound if translocation of gut bacteria and endotoxins contribute to the development of systemic sepsis and multi-organ failure (**Kramer and Wallfisch, 1992**).

Microcirculatory failure and rapid deterioration of organ function related to endotoxaemia and septic shock are common clinical features of multiple system organ failure following major trauma. In this context, **Kreimeier et al. (1991)** recently showed experimentally that small - volume resuscitation, by means of hypertonic saline - dextran, restors microcirculatory failure in sepsis and endotoxaemia most effectively by maintenance of the hyperdynamic circulatory state and a permanently high blood flow to the heart, kidney and splanchnic organs.

Hypertonic solutions and burn injury :

New studies have been performed on the use of hypertonic saline for the treatment of circulatory shock in the presence of increased capillary permeability as in burn injury and sepsis. **Tokyay et al. (1992)** found that an initial bolus treatment of HSD in burn-injured pigs resulted in better sustained DO_2 and VO_2 in the mesenteric circulation. One possible explanation for improved blood flow may be attributed to a reversal of shock-induced endothelial swelling by HSD.

Chimazaki et al. (1991) compared isotonic resuscitation to hypertonic NaCl lactate solutions in the first 24 h in burn-injured humans, hypertonic saline lactate normalized extracellular fluid volume better and resulted in better respiratory function, more normal plasma volumes and a higher plasma volume : extracellular fluid volume ratio, 3 - 5 days post-burn. Recent research in burn shock has suggested that specific inflammatory mediators are responsible for gut ischemia. It has been reported that burn injured pigs exhibit an initial intense and sustained fall in mesenteric blood flow during the first 24 post burn hours despite normalization of cardiac out-put using the isotonic LR solution, while, initial changes in mesenteric vascular resistance were prevented with treatment during the burn using OKY 46, a thromboxane synthetase inhibitor. In another study the sustained fall in mesenteric

blood flow was prevented by a 10 ml/kg infusion of HSD administrated 30 min post-burn (**Tokyay et al., 1992**). Both studies showed decreased rate of translocation of bacteria, and prevention of persistent arteriolar constriction after hypovolemia in the terminal ileum when HSD was used for resuscitation of burn shock.

Hypertonic solutions and head injury :

The interaction of severe blood loss and cranial trauma with small volume hypertonic resuscitation was first examined by **Prough et al. (1985).**

Recent data in which the haemorrhage - cranial trauma combination was treated in canine or porcine models with small - volume hypertonic or large - volume isotonic resuscitation indicate that small volume hypertonic resuscitation is beneficial because haemodynamic improvement is associated with lowered intracranial pressure **(Prough et al., 1991).** However, **Battistella and Wisner (1991)** recently reported that haemorrhaged rats, subjected to mechanical brain trauma, had increased brain water in the injured hemisphere regardless of the resuscitation fluid but showed lower brain water in the uninjuried brain if resuscitated with a hyper-osmotic solution.

Prough et al. (1991) reported that HS lowered intracranial pressure more than isotonic saline and produce more improvement in both global and regional cerebral blood flow. Equal cerebral perfusion pressures occurred in both groups, but better cerebral blood flow with hypertonic saline suggested a direct cerebral arteriolar dilatory effect of hypertonicity.

It has been demonstrated that the incidence of mortality and morbidity resulting from severe head trauma is strongly related to elevated ICP and hypotension (**Marmarou et al., 1991).** Administration of small volumes (250 ml) of 7.5% NaCl/dextran 70 before hospitalization increased the blood pressure of severely injured patients more effectively than lactated Ringer's solution did and showed a tendency towards improving survival in the patients with severe head injury (**Vasser et al., 1991).** Currently, the concept of initial management of head injury involves the use of hyperosmotic saline containing solutions as "fluid of choice" **(White and Likavec, 1992).**

MECHANISM OF ACTION OF SMALL-VOLUME RESUSCITATION

1. Mobilization of endogenous fluid :

Small-volume resuscitation consists of the physiological mechanisms of action operational at the microcirculatory level. The key feature is the instantaneous increase of plasma volume by mobilization of endogenous fluid along osmotic gradients across membranes **(Kreimeir and Messmer, 1991).**

According to **Mazzoni et al. (1988)** 7.5% saline/6% dextran 70 solution, given over 10 seconds, in an amount equivalent to one-seventh of a 20% blood loss, will be sufficient to re-establish normal blood volume within 1 min.

Vasser and Holcroft (1992) estimated that administration of 250 ml of 7.5% Nacl/6% dextran 70 to a 70-Kg patient who has suffered a two-liters blood loss will result in plasma volume expantion of at least 700 ml. To achieve equivalent plasma volume expansion with lactated ringer's solution, these authors estimated that 2.8 liters of solution would be necessary.

2. Effect on the endothelium and cell volume changes :

During small-volume resuscitation, endogenous fluid is mobilized first of all from the microvascular endothelium and the red blood cells **(Mazzoni et al., 1990).** With the most pronounced effect taking place in those capillary districts with swollen endothelium; the more swollen the endothelium, the greater the effect of hyperosmotic solutions in terms of the reduction of hydraulic resistance and hence improvement of tissue perfusion **(Mazzoni et al., 1988).**

Mazzoni et al. (1989) have investigated the volume changes of endothelial cell monolayers on exposure to anisotonic media. From their studies it can be deduced that the increase in plasma osmolality to 460 m. osmol/Kg, which transiently occurred at the end of bolus infusion of 7.5% saline should result in shrinkage of endothelial cell volume by 20%.

Moreover **Nolte et al. (1992)** have published noval data on the leukocyte/endothelial interaction of hyperosmotic-hyperonocotic dextran solution after ischemia/reperfusion injury in the hamster dorsal skin fold model. They demonstrated that, following 4 h., of ischemia and reperfusion of striated muscle, the number of leukocytes adhering to the endothelium of post-capillary venules was significantly reduced for 24 h.,

after a bolus infusion of 7.2% Na cl/10% dextran 60. In addition, hyperosmolar saline dextran effectively attenuated macromolecular leakage and reduced capillary endothelial swelling as assessed by measurements of capillary lumenal diameters.

3. Cell metabolism and membrane-bound transport systems:

Following studies on skeletal muscle in rats suffering from hemorrhagic shock, **Nakayama et al. (1985)** reported that the fluid shifts across cell membranes induced by resuscitating with 0.4 ml of a 7.5% solution of Nacl resulted in normalization of the cell volume and the intracellular concentrations of sodium and chloride, together with the restoration of the normal membrane resting potential by regulation of Na^+, K^+ and Cl^- transport.

4. Release of mediators :

Recent data from animal studies reveal that the increase in cardiac output and restoration of peripheral blood flow is mediated by the instantaneous release of vasodilator substances of eicosanoid origin **(Marti-cabrera et al., 1991),** particularly by prostacyclin together with an enhanced 6-keto-$PGF_{1\alpha}$/thromboxan B_2 ratio **(Rabinovici et al., 1992).** Also, studies of endothelial cells demonstrated the link between shear-stress (blood-flow) and the production of nitric oxide **(Buga et al., 1991).**

Wade et al. (1991) found that, following small volume resuscitation, the levels of plasma adrenocorticotropic hormone, cortisol and aldosterone decreased, although this effect was primarily a result of hemodilution associated with the expantion of plasma volume. In contrast, the reduction in concentrations of plasma norepinephrine, epinephrine, lysine, vasopressin and plasma renin was greater than could be attributed to hemodilution alone, which indicates that altered hormone release plays a role in the cardiovascular response to this mode of resuscitation.

5. Further mechanisms involved :

Besides global peripheral arterial vasodilatation other mechanisms are considered of importance for the restoration of cardiac output and nutritional blood flow. Myocardial stimulation, central nervous system stimulation, neurogenic reflex mechanisms, improvement of blood fluidity and re-establishment of spontaneous arteriolar vasomotion **(Kreimeier et al., 1990).**

Extracellular osmolality is known to affect myocardial contractility, and the positive effects on cardiac mechanics, may be causally related to the intracellular shift in calcium ions and reduction of myocardial oedema. **Haim et al. (1992)** have given evidence that increasing

concentration of Na^+ had a positive inotropic effect at an osmolality range of 240 - 320 m. osmol, whereas higher concentrations of Na^+ had a negative inotropic effect.

Early in **1981 Lopes et al.,** had suggested that a vagal reflex, triggered by stimulation of osmoreceptors in the pulmonary circulation, should play an essential role in the effectiveness of hyper osmotic resuscitation.

SPECTRUM OF INDICATIONS OF HYPERTONIC SALINE SOLUTION

Beside the improvement of haemodynamics and microcirculation in haemorrhagic shock in trauma patients, hyperosmotic saline resuscitation has been shown to reduce bacterial translocation in rats subjected to haemorrhagic shock and this has been attributed to prevention of gut hypoperfusion **(Reed et al., 1991).** Therefore, small volume resuscitation may be useful in critically ill patients known to be at risk of developing MSOF on the basis of compromised blood flow in the gut mucosa **(Kreimeier et al., 1993).**

Hyperosmotic saline dextran has been suggested to be beneficial after burn injury through the reversal of microcirculatory disturbances, and attenuation of oxidant-induced systemic and mesenteric lipid peroxidation, which might be linked to the alterations of the concentration and activity of intracellular Na^+, and changes in water content **(Chiao et al., 1992).**

The concept of small-volume resuscitation has been demonstrated to be both feasible and effective in primary resuscitation of trauma patients undergoing helicopter transport, in the emergency room, in

cardiac surgery, in critically ill patients and even for the treatment of acute myocardial infarction **(Ramires et al., 1992).**

In addition, the effect of a 5% saline solution for fluid preloading before lumbar extradural anesthesia and the use of 7.2% NaCl/6% hydroxy ethyl starch for doubling pulmonary capillary wedge pressure (PCWP) after induction of anaesthesia in patients undergoing cardiac surgery, have been investigated. In both trails the hyperosmotic saline solution was judged to be beneficial, especially for those situations when rapid fluid preloading is desired without excess free water administration **(Boldt et al., 1991).**

SAFETY AND POSSIBLE ADVERSE EFFECTS OF HYPERTONIC SALINE SOLUTION

The beneficial haemodynamic effects of hypertonic solutions must be weighed against their potentially deleterious effects. Bolus infusion of a hyperosmotic solution of NaCl (> 10%) into a peripheral vein has been shown to result in significant haemolysis, whereas hyperosmotic solutions of 7.0 - 7.5% NaCl are regarded as safe **(Rocha et al., 1990).**

The efficacy and safety of 7.2 - 7.5% NaCl in combination with 6% dextran 60/70, has been demonstrated in nearly 700 patients and no phlebitis has been observed at the injection site, which in most cases was cubital vein **(Vassar and Holcroft, 1992)**.

Serum osmolarities above 350 mosmol/L have been reported in some patients who received either 7.5% NaCl/4-6% dextran 70 or ringer's lactate. Most of these patients has serum ethanol concentrations of at least 39 nmol/liter accounting for 36 mosmol of the total serum osmolality measured. Non of these patients, showed any acute clinical signs of hyperosmolality **(Vassar et al., 1992)**. However, serum osmolality decreased within 4-8 h after bolus infusion of hypertonic saline solution **(Matox et al., 1991).**

Infusion of hyperosmotic solutions may provoke electrolyte imbalance. In a controlled clinical study in trauma patients, mean serum sodium concentration was 9 mEq/L higher in the treatment group than in the control group at the time of arrival in the emergency room, however hypernatraemia occurred without neurological symptoms in two out of 55 patients. Also neuropathological signs of central pontine myelolysis were not found in any of the patients who died **(Vassar et al., 1992).**

Other potential complications of small volume resuscitation include risks of hypokalaemia due to enhanced loss of potassium in the urine, particularly in cases of pre-existing dehydration. Also haemolysis and haemoglobinuria, altered clotting times and platelet aggregation had been linked to the colloid component **(Kreimeier et al., 1993).**

MATERIAL AND METHODS

The present study has been carried out in the Faculty of Medicine, Zagazig University, after approval of the council committee.

Experimental protocol :

This study was done on 60 Albino rats of local strain of either sex weighining 180 to 240 gm. The rats were divided into 6 equal groups each containing 10. Controlled haemorrhagic shock was done by arteriotomy bleeding through a catheter introduced in the caroted artery. 30% of the calculated blood volume (8.0 ml/100 gm) was sheded over 30 minutes (2.4 ml/100 gm) into an empty heparinized syrenge. The controlled hemorrhage was followed by resuscitation using different fluid solutions as following (Figs. 3 and 4).

All rats used in the present study were left for one hour after cannulation for haemodynamic stabilization and they were divided into 6 groups :

Fig. (3) : Inducing shock by haemorrhage.

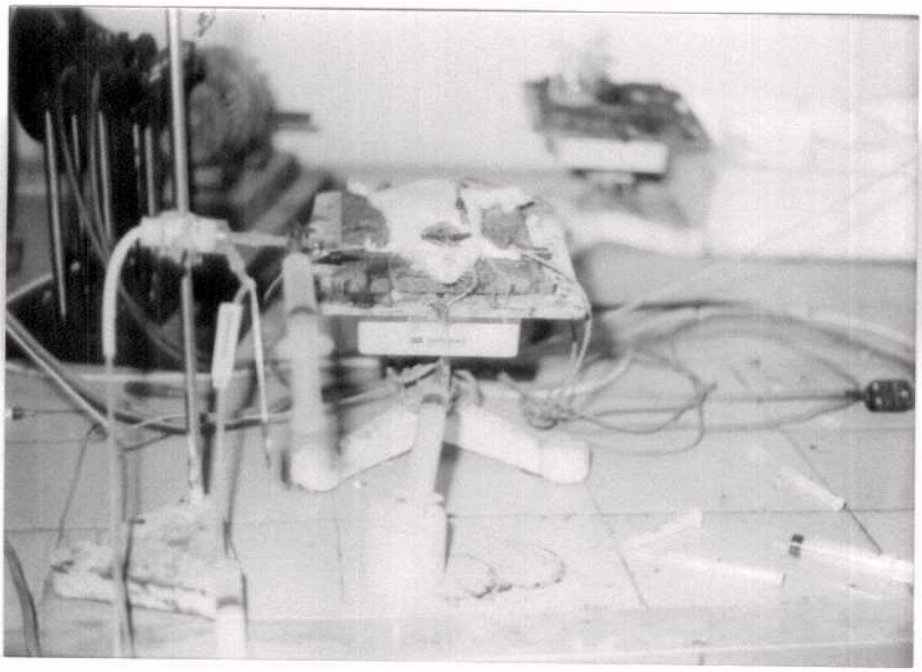


Fig. (4) : Resuscitation with solutions.

Group 1 (sham operated group) :

This group was used for the study of the effect of anaesthesia, cannulation and food and water deprevation on the animal and to exclude any large effects of anaesthesia on the haemodynamics, body electrolytes and blood gases. No bleeding was done in this group.

Group 2 (the control group):

This group was used for studying the effect of haemorrhage on blood pressure, heart rate, myocardial contractility, blood gases, serum electrolytes, haematocrit and the mean corpuscular volume and compare this effect with that after resuscitation using different solutions in the other groups. No resuscitation was done in this group after the induced shock.

Group 3 :

This group was used for the study of the effect of resuscitation with Ringer lactate, on the shocked rats, and comparing it with the other solutions. Ringer lactate 6 ml/100 gm was given over 15 minutes. The resuscitation started 30 minutes after cessation of haemorrhage.

Group 4 :

The rats in this group were resuscitated using hypertonic saline

solution (NaCl 7.5%) 0.6 ml/100 gm given over 5 min. The resuscitation started 30 minutes after cessation of hemorrhage.

Group 5:

The rats in this group were resuscitated with 6% dextran 70, 0.6 ml/100 gm given over 5 minutes from cessation of bleeding.

Group 6 :

The rats in this group were resuscitated with a combination of NaCl 7.5% and 6% dextran 70 in equal volumes for both (hypertonic saline/dextran "HSD") at a total dose of 0.6 ml/100 gm given over 5 minutes, resuscitation started 30 minutes after cessation of the controlled bleeding.

Drugs and solutions used in alphabetic order :

1. 6% dextran 70 (Arab Otsuka Co. Egypt).

   Used for resuscitation of the rats after the induced shock. It was given in dose of 0.6 ml/100 gm over 5 minutes.

2. Ethylcarbamate (urethane) powder, (prolabo, Paris).

   It is readily soluble in water and the dose used 1.75 - 2.0 gm/kg given by I.P. injection as 25% freshly prepared aqueous solution for anaesthetizing the experimental animal (**Ghosh, 1971).**

3. Heparine 1 ml ampoules of 5000 Iu/ml (Nile Co. Egypt).

   The concentration used to inhibit blood coagulation in the arterial and venous cannulae was 16 I.u/ml **(Tuttle and Mills, 1975).**

4. Hypertonic saline "NaCl 7.5%" (Arab. Otsuka Co. Egypt). Used for resuscitation of rats after the induced shock. It was given in a dose of 0.6 ml/100 gm over 5 minutes.

5. Hypertonic saline, Dextran (Arab Otsukco Egypt).

   It is a combination of hypertonic saline (7.5%) and 6% dextran 70 1 : 1. It was used for resuscitation of rats after the induced haemorrhagic shock. It was used in a dose of 0.6 ml / 100 gm given over 5 minutes.

6. Ringer's lactate (El-Nasr Co. Egypt).

   Used for resuscitation of the shocked rats after the induced haemorrhage in a dose of 6 ml/100 gm given over 15 minutes.

The equipments :

1. One 4-channel oscillograph MD4 (Bioscience London).
2. One FC 123 ECG facility coupler.

3. One ECG limb cable.
4. Two FC137 strain gauge couplers.
5. Two PT400 blood pressure transducers.
6. Rat arterial and venous cannulae (polyethylene inner diameter 0.5 mm).
7. Surgical instruments.
8. Mercury sphygmomanometer.
9. 500 ml capacity glass bottle with tight rubber stopper. Through one of the two holes in the stopper, an L-shaped rigid glass tube forced to enter until it reached 0.5 cm from the bottom, and through the other hole, one limb of a T-shaped rigid glass tube forced just to pass through the rubber cover.
10. Tuberculin syringe and 2.5, 10 ml capacity syringes.
11. Infusion sets, with their rubber pieces and clamps, used for doing various connections during the experiments.
12. Weight scale.
13. 3-way small polyethylene values.

Preparation for the experiments :

A. Preparation of the recording system :

1. The ECG limb cable was attached to the FC 123 ECG facility coupler which was fixed to one of the 4-channels of the

oscillograph MD4 (Fig. 5).

2. The PT400 blood pressure transducer was connected to the FC 137 strain gauge coupler which was fixed to another channel of the oscillograph.
3. Another PT400 blood pressure transducer was connected to another FC 137 strain gauge coupler which was fixed to a third channel of the oscillograph.
4. About 10 cm length polyethylene tube with a clamp was connected to one side limb of the PT 400 transducer. The other limb of the transducer was connected through polyethylene tube with a clamp to the arterial cannula.
5. The 500 ml capacity glass bottle is filled with normal saline solution containing 16 Iu/ml heparin (**Tuttle and Mills, 1975**). The pump of the sphygmomanometer was connected to one limb of the T-shaped glass tube fitted in the bottle, while the other limb is connected to the sphygmomamometer (Fig. 6). The L-shaped glass tube was connected to the PT400 pressure transuser stopper was connected to the side limb of the transducer, all valves were opened, the pressure inside the bottle was raised by pressing on the pump so that the solution would be pushed to fill the connections to the transducer and the valve of the other limb of the transducer was re closed. Calibration of the blood pressure transducer was

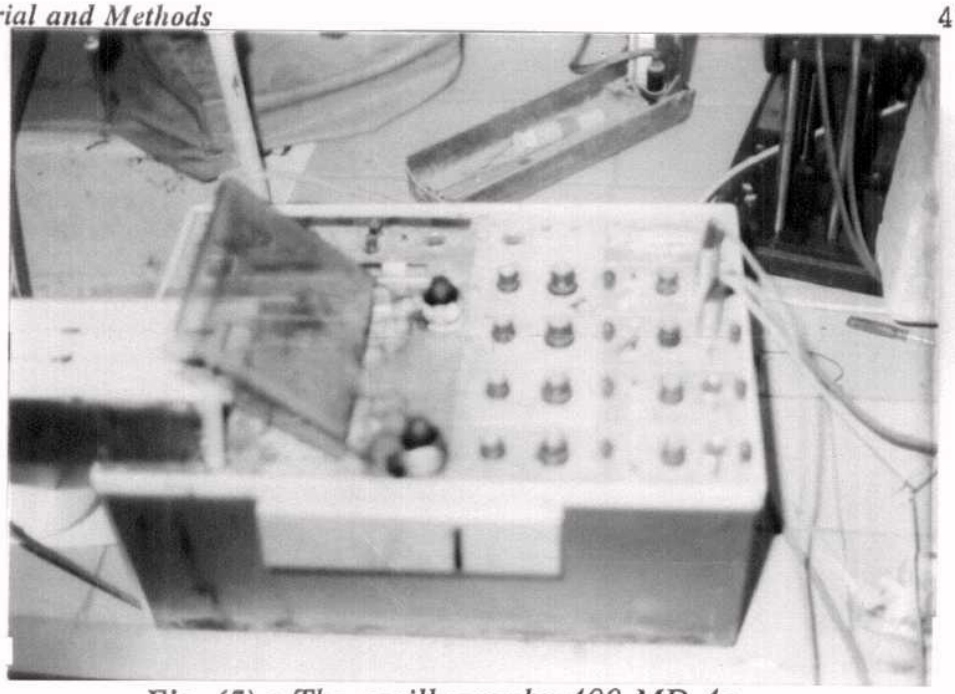


Fig. (5) : The oscillography 400 MD 4c.

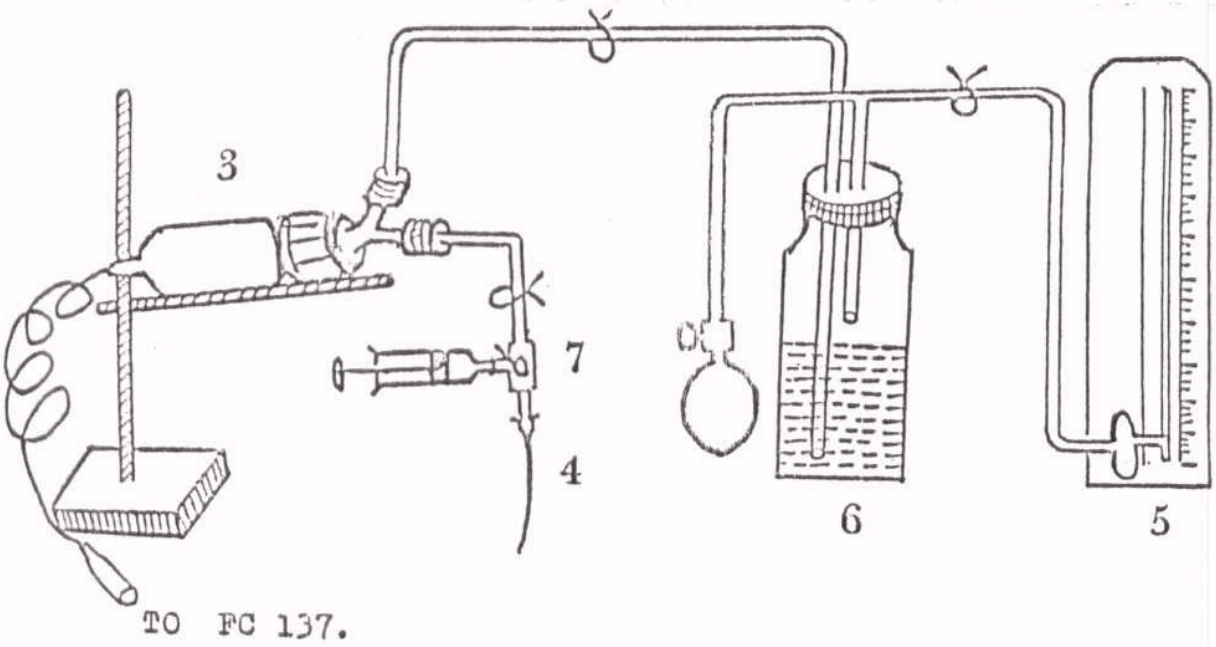


Fig. (6) : The apparatus used for the calibration of the bP in terms of mmHg.

done by gradual elevation of the pressure in the bottle, thereby, in the mercury manometer, starting from zero to 200 mmHg (20, 40, 60 .... etc) (Fig. 7), after that all valves were closed and the transducer was disconnected from the bottle. Calibration was done both before and after the experiments.

B. Preparation of the animal :

1. Anaesthesia of the animal :

The rat was anaesthetized with urethane (ethyl carbamate, Porlabo, Paris), in a dose of 1.75 - 2.0 gm/kg body weight injected into the peritoneal cavity (i.p) as 25% aqueous solution freshly prepared **(Gosh, 1971).**

2. Intra-arterial cannulation and record of the systemic arterial blood pressure :

After maintenance of anaesthesia, the animal was placed on a board in the supine position. The four limbs were extended and fixed to the side of the board. dissection was started by shaving the front of neck of the animal. A midline incision was made on the skin of the neck starting from the lower end of larynx to the upper end of thorax. Muscles were separated along the midline, trachea was exposed and a transverse cut was made in between

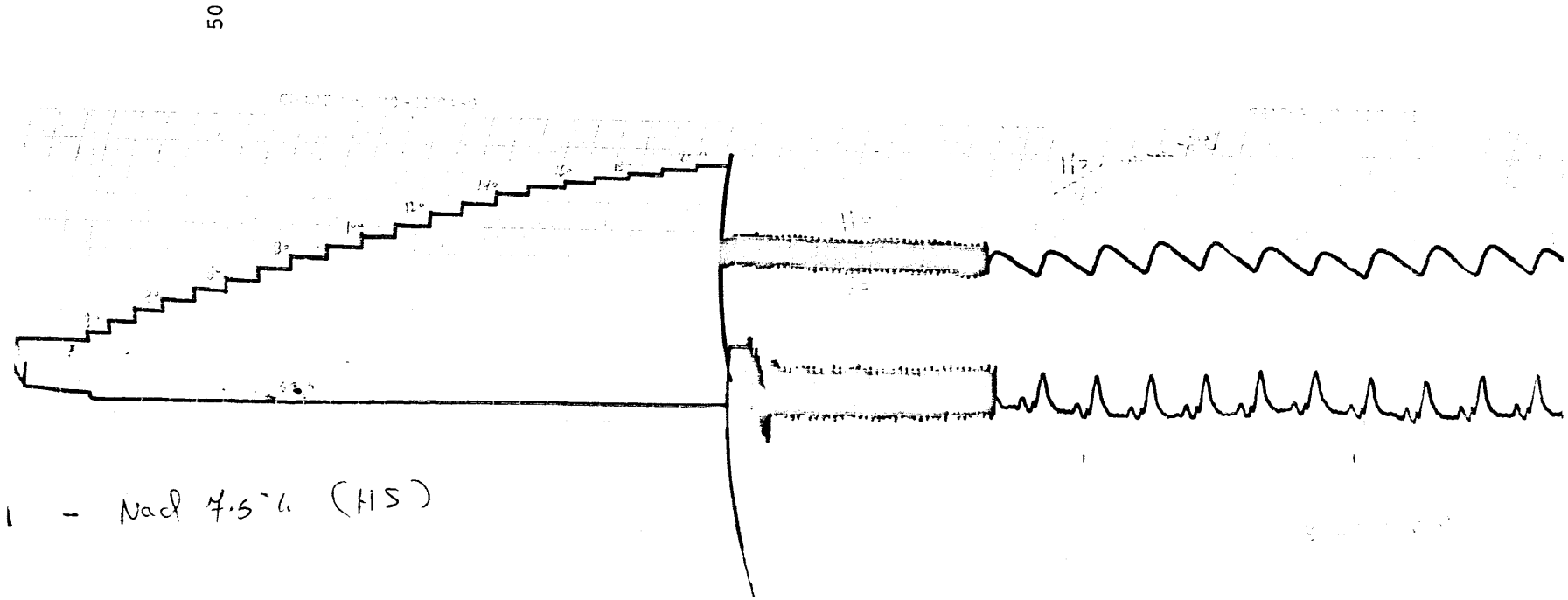


Fig. (7) : Scale for the calibrated blood pressure transducer.

two rings for the introduction of the tracheal cannula that was then held in position by a twin ligature.

The left common carotid artery was exposed, dissected and cleared for a sufficient length, it was ligtad as near to the head as possible. A pulldog clamp was applied on the carotid artery as proximal to the chest as possible and a thread was passed around the artery, a cut was made on the artery, just proximal to the first ligature, through which the already heparinized saline filled arterial cannula was inserted and directed toward the heart and firmly fixed by ligation the thread already in position **(Ghosh, 1971).**

The pressure in the manometer was then increased to about 150 mmHg (slightly more than the expected level of the systolic blood pressure of the rat) and the 3-way valve turned so that the blood pressure transducer remained in communication only with the cannula. By removing of the pulldog clamp and by switching on the apparatus, the systolic and diastolic blood pressure were traced on the paper chart of the oscillograph at a speed of 0.25 mm/second.

3. Cannulation of the right external jugular vein :

This vein was exposed just under the skin at the side of the neck guided by its surface anatomy (the line extended from the angle of the right mandible to the right sternoclavicular junction). The venous cannula, fixed to a tuberculin syringe filled with normal saline containing 16 I.U/ml heparin, was inserted into the vein in the same fashion as into the artery except that the pulldog clamp was first applied proximally, and a ligature tied a little distally while the vein is full of blood. After the cannula was fixed in position, the pulldog clamp was removed and 0.2 ml of the content of the syringe was injected to prevent clot formation. This tube was used similarly for the injection of all intravenous resuscitation solutions used throughout the experiment.

4. Recording of the electrocardiogram :

The ECG limb cable was attached through hypodermic needles inserted and fixed subcutaneously, in shoulders and groins for the limb leads and to the chest wall over the apex of the heart for the chest lead. Thr FC 123 was switched on lead II that gives good signals for analysis of ECG. The paper chart speed for recording the ECG by the oscillograph was 50 mm/second, calculation of the heart rate/minute was carried out using a

standard ECG paper chart with a standard speed 50 mm/second dividing "600" by the number of big squares between two successive P or R waves (**Gay, 1965**).

5. Measurement of the myocardial contractility :

The contractility index was determined from the arterial pressure waveform (contractility index = dP/dT) (Fig. 8). (**Aitkenhead and Smith, 1990**).

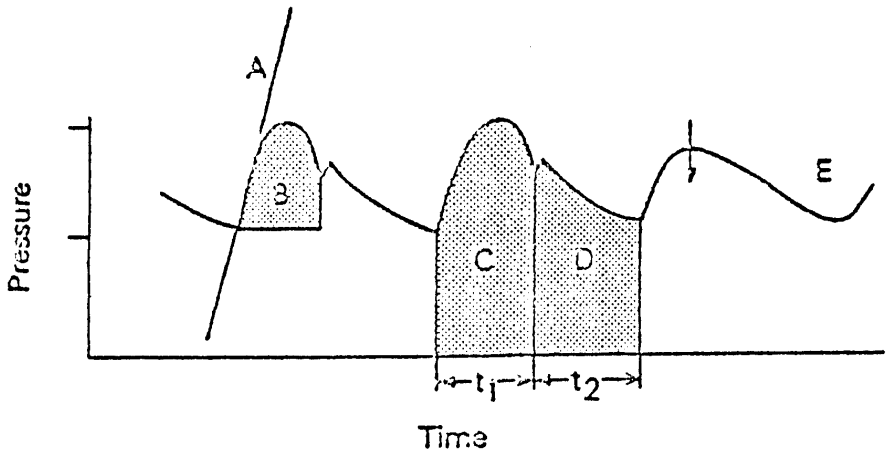


Fig. (8) : Information to be gained from the arterial pressure signal.

Visible sign	*Physiological effect*
A. Rate of pressure increase	myocardial contractility
B. Area under pulse pressure	stroke volume
C. Systolic pressure x time (t_1)	myocardial oxygen consumption
D. Diastolic pressure x time (t_2)	myocardial oxygen supply
E. Loss of waveform detail	catheter occlusion

(Atkinson and Rushman, 1987)

6. Measurement of hematocrite and mean corpuscular volume:

The blood samples were collected in heparinized tubes and the hematocrite % and the mean corpuscular volume were measured before bleeding and 4 hours after resuscitation using a computerized analyzer (coulter microdef 18, laser).

7. Measurement of serum Na and K levels :

The blood samples were collected in heparinized syringe. Serum Na and K levels were measured before bleeding and 4 hours after resuscitation by KNA_2 analyzer.

8. Measurement of blood gases and bicarbonate level :

Blood samples were collected in heparinized glass syrenge, and kept in crushed ice till measurement was done using the blood gas analyzer ABL 330.

The mean arterial blood pressure, pulse rate, and contractility index were recorded before bleeding, 30 minutes after haemorrhage, and 5 minutes, 30 minutes, 1, 2, 3, and 4 hours after resuscitation.

Na^+ and K^+ levels, hematocrite %, mean corpuscular volume, and blood gases were measured before bleeding and 4 hours after resuscitation.

Statistical analysis :

Data were collected, tabulated, analyzed and interpreted by the suitable statistical technique according to **Rebeca and Clinton (1992) and WHO (1994).**

Then the data were manipulated by using IBM compatible software EPI. INFO version 6.2 for epidemiological study adopted by **WHO (1994).**

I. Mean Arterial Pressure (MAP) :

$$MAP = DBP + \frac{SBP - DBP}{3}$$

Where :

DBP = Diastolic blood pressure
SBP = Systolic blood pressure

II. Arithmetic mean (X) :

$$X = \frac{\Sigma X}{n}$$

Where :

Σx = Sum of individual data
n = Number of individual data

III. Standard deviation (SD) :

Where :

ΣX = *sum of figures*
$\Sigma(X^2)$ = *sum of squares of the figures*

$$S.D=\sqrt{\frac{E(X)^2-\frac{\Sigma X)^2}{n}}{n-1}}$$

IV. Student "t" test :

- Used to test for the significance between two means according to the following formula :

$$t=\frac{X_1 - X_2}{\sqrt{\frac{(SD_1)^2}{n_1}+\frac{(SD_2)^2}{n_2}}}$$

Where :

X_1 , X_2 : The mean of the first and second groups respectively.
n_1 , n_2 : The number of first and second groups respectively.
SD_1 , SD_2 : The standard deviation of the first and second groups respectively.

$P > 0.05$ Not significant
$P < 0.05$ Significant
$P < 0.001$ Very highly significant

VI. Analysis of Variance (F-test) :

$$\text{C.F. (correction factor)} = \frac{(\Sigma x_1 + \Sigma x_2 + \Sigma x_3)^2}{n\ (\text{Total})}$$

$$\text{Total SS (Total sum of squares)} = [\Sigma x_1^2 + \Sigma x_2^2 + \Sigma x_3^2] - \text{C.F.}$$

$$\text{Between SS} = \left[\frac{(\Sigma x_1)^2}{n_1} + \frac{(\Sigma x_2)^2}{n_2} + \frac{(\Sigma x_3)^2}{n_3}\right] - \text{C.F.}$$

Within SS = Total SS - Between SS

$$\text{M.S. between (mean square between)} = \frac{\text{Between SS}}{\text{Small d.f.}}$$

Where : small d.f. = The number of groups -1

$$\text{M.S. within (mean square within)} = \frac{\text{within SS}}{\text{Large d.f.}}$$

Where : large d.f. = The total number of patients - number of groups

$$F = \frac{\text{MS between}}{\text{MS within}}$$

The significance of "F" was obtained from "*f*" tables.

VII. Least significance difference (LSD) :

$$LSD = t\sqrt{MS\ within\ (\frac{1}{n_1}) + (\frac{1}{n_2})}$$

Where :

"t" = The value of "t" at large d.f. (n_1-2) in the "t" table then we calculate; $x_1 - x_2$ (The difference between the two mean values) if :

less than LSD at 0.05 → Non-significant (N.S.).

more than LSD at 0.05 →Significant (S)

more than LSD at 0.01 → High significant (H.S)

RESULTS

The present study demonstrated that there were no significant differences in the mean arterial blood pressure, heart rate and contractility index when recorded just after anaesthesia compared to 1,2,3,4, hours, after induction of anaesthesia (Table 1).

Controlled bleeding (30% of the calculated blood volume) produced significant ($P < 0.001$) decrease in the mean arterial pressure, heart rate and contractility index when the parameters were recorded 30' minutes, 1,2,3 and 4 hours after bleeding and compaired to values before bleeding. However, no significant difference between the values of each parameter if compaired at the formentioned different times (Table 2).

Resuscitation with different solutions (Ringer's lactate, dextran, hypertonic saline and hypertonic saline - dextran) produced significant ($P < 0.001$) increase in the mean arterial pressure when recorded 5 and 30 minutes, 1,2,3 and 4 hours following resuscitation and compaired to values after bleeding (Table 3).

Comparison of the effect of different solutions on the mean arterial blood pressure demonstrated that both hypertonic saline (HS) solution and hypertonic saline dextran (HSD) solution produce more significant ($P < 0.05$) increase in this parameter when compaired to resuscitation with either dextran 70 alone or Ringer's lactate solution. Comparison of the effect of hypertonic saline (HS) with the hypertonic saline dextran (HSD) on the mean arterial blood pressure revealed no significant difference between them (Tables 3 and Figs. 9 and 10).

Resuscitation with the hypertonic saline and hypertonic saline - dextran produced significant ($P < 0.05$) increase in the heart rate when recorded 5 and 30 minutes, 1,2,3 and 4 hours following resuscitation, although, resuscitation with Ringer's lactate and dextran produced no significant increase in the heart rate when recorded at 5 minutes following resuscitation, hoever, it produced significant ($P < 0.05$) increase when recorded at 30' minutes, 1,2,3, and 4 hours following resuscitation when compaired to values after bleeding (Table 4 and Figure 11).

Comparison of the effect of resuscitation with the different solutions on the heart rate demonstrated that both hypertonic saline and hypertonic saline dextran produced more significant increase in the heart

rate when recorded 5 minutes following resuscitation when compaired with Ringer's lactate and dextran at the same time. But there is no significant differences inbetween the effect of the 4 solutions when compaired at 30' minutes, 1,2,3 and 4 hours following resuscitation. Comparison of the effect of the hypertonic saline and hypertonic saline dextran revealed no significant different between them at all recording time, following resuscitation (Table 4 and Figure 11).

Resuscitation with the different solutions used, produced significant ($P < 0.01$) increase in the contractility index when recorded at 5 and 30 minutes, 1,2,3 and 4 hours following resuscitation (Table 5 and Figure 12) comparison of the effect of the different solutions on the contractility index demonstrated that both the hypertonic saline (HS) solution and the hypertonic saline Dextran (HSD) solution produced more significant ($P < 0.05$) increase in this parameter when compaired to resuscitation with either dextran 70 (Dex) alone or Ringer's lactate solution. Comparison of the effect of hypertonic saline (HS) with the hypertonic saline - dextran (HSD) on the contractility index revealed no significant difference between them (Table 5 and Figure 12).

In the shame operated group, recording of the blood pH, arterial oxygen tension (PaO_2), arterial carbon dioxide tension ($PaCO_2$) and

plasma bicarbonate level (HCO_3), just after anaesthesia and 4 hours later revealed no significant changes in each of these parameters (Table 6).

The induced hemorrhagic shock with controlled bleeding (30% of the calculated blood volume) produced significant ($P < 0.05$) decrease in the blood pH, arterial carbon dioxide tension ($PaCO_2$), and plasma bicarbonate level (HCO_3), and produced significant ($P < 0.05$) increase in the arterial oxygen tension (PaO_2) when recorded at 4 hours after bleeding and compaired to the values recorded before bleeding (Table 7).

Resuscitation of the controlled hemorrhagic shock with the different solutions produced significant ($P < 0.05$) decrease in the blood pH, when recorded 4 hours after resuscitation and compaired with value of pH before bleeding (Table 8 and Fig. 13) comparison of the effect of resuscitation with the different solutions on the pH demonstrates more significant ($P < 0.05$) decrease in the pH when Renger's lactate and dextran solutions were used for resuscitation than when hypertonic saline and hypertonic saline dextran were used. Comparison of the hypertonic saline with the hypertonic saline-dextran revealed no significant difference between their effect on the blood pH (Table 4 and Figure 13).

Resuscitation with the different solutions produced significant decrease in the arterial carbon dioxide tension ($PaCO_2$) when recorded 4 hours after resuscitation and compaired to the values before bleeding (Table 9 and Figure 14).

Comparison of the effect of the resuscitation with the different solutions on the arterial carbon dioxide tension ($PaCO_2$) 4 hours after resuscitation revealed more significant ($P < 0.05$) decrease in the ($PaCO_2$) when dextran 70 alone and ringer's lactate were used for resuscitation than when, hypertonic saline or hypertonic saline dextran were used. Comparing the effect of resuscitation with hypertonic saline (HS) to hypertonic saline dextran (HSD) revealed no significant difference on the arterial carbon dioxide tension ($PaCO_2$) when recorded 4h after resuscitation (Table 9 and Figure 14).

Resuscitation of the controlled hemorrhagic shock with Renger's lactate and dextran 70 alone produced significant ($P < 0.05$) increase in the arterial oxygen tension (PaO_2) when recorded 4 hours after resuscitation and compaired to the values of (PaO_2) before bleeding. While the resuscitation with the hypertonic saline (HS) and the hypertonic saline dextran (HSD) solutions produced no significant change in the (PaO_2) at the same time after resuscitation. comparison of the

effect of the resuscitation with Ringer's lactate (RL) and dextran 70 (Dex 70) on the PaO_2 revealed no significant differences between them (Table 10).

Resuscitation after the controlled hemorrhagic shock with the different resuscitating solution produced significant ($P < 0.05$) decrease in the serum bicarbonate (HCO_3) level with all types of resuscitating solutions when compaired to values before bleeding (Table 11 and Figure 15) comparison of the effect of resuscitation with the different solutions on the serum bicarbonate revealed no significant difference between them (Table 11 and Fig. 15).

There was no change in the sodium and potassium level when recorded 4 hours after anaesthesia and compaired to values recorded just after anaesthesia (Table 12).

The induced hemorrhagic shock by sheding of 30% of the calculated blood volume produced significant ($P < 0.05$) increase in the serum level of sodium and potassium when measured 4 hours after bleeding and compaired to values before bleeding (Table 13).

Resuscitation with hypertonic saline (HS) and hypertonic saline dextran (HSD) produced significant ($P < 0.001$) increase int he sodium level in plasma, while resuscitation with dextran alone and Ringer's lactate produced no significant change in sodium level when measured 4 hours after resuscitation and compaired to the values recorded before bleeding (Table 14) comparison of the effect of resuscitation, with hypertonic saline and hypertonic saline dextran revealed no significant difference between them (Table 14 and Fig. 16).

Resuscitation with Ringer's lactate (RL), dextran (Dex) alone and with hypertonic saline-dextran (HSD) produced significant ($P < 0.05$) increase in the potassium level in plasma when measured 4 hours after resuscitation when compaired to values before bleeding. On the other hand, hypertonic saline (HS) produced no significant change in potassium level when measured at the same time and compaired to the values before bleeding (Table 15 and Fig. 17). Comparison of the effect of the (RL, HSD, Dex) solutions on serum potassium 4 hours after resuscitation revealed no significant difference in between them (Table 15).

Anaesthesia produced no significant change in the hematocrit and mean corpuscular volume when measured 4 hours offer anaesthesia and compaired to values just after anaesthesia (Table 16).

Hemorrhagic shock (30% bleeding) produced significant ($P < 0.05$) decrease in hematocrit percentage and significant ($P < 0.01$) increase in the mean corpuscular volume when these variables measured 4 hours after the induced bleeding and compaired to values before bleeding (Table 17).

Resuscitation with the different types of solutions produced significant ($P < 0.001$) decrease in hematocrit when measured 4 hours after resuscitation and compaired to the values before bleeding (Table 18).

The comparison between the effect of resuscitation with the different solutions on hematocrite revealed that there is more significant ($P < 0.05$) decrease in the hematocrite when hypertonic saline (HS) and hypertonic saline dextran (HSD) were used than when Ringer's lactate and dextran 70 alone were used. Comparison between the effect of resuscitation with hypertonic saline and hypertonic saline dextran on hematocrit when measured at 4 hours of resuscitation revealed no significant difference (Table 18 and Figure 18).

Resuscitation with hypertonic saline (HS) and hypertonic saline dextran (HSD) solutions produced significant ($P < 0.01$) decrease in the

mean corpuscular volume when measured 4 hours after resuscitation and compaired to the values before bleeding. On the other hand, resuscitation with Ringer's lactate (RL) and dextran (Dex) solutions produced no significant change in the mean corpuscular volume when measured at the same time after resuscitation (Table 19 and Fig. 19).

Comparing the effect of resuscitation with hypertonic saline and hypertonic saline dextran on the mean corpuscular volume revealed no significant difference between them (Table 19 and Fig. 19).

Table (1) : Changes (Mean ± SD) in mean arterial blood pressure (mmHg) heart rate (beat/min) and contractivity index (mmHg second) in response to anaesthesia in sham operated group of rats "group 1".

	Mean ± SD				
	After induction of anaesthesia	**After anaesthesia**			
		1h.	2h.	3h.	4h.
Mean arterial blood pressure (mmHg)	98.0 ±4.94	96.8 ±6.9	96.6 ±7.0	95.9 ±6.6	97.4 ±5.5
Heart rate beat/minute	286.0 ±18.9	286.0 ±21.2	287 ±21.6	284 ±22.2	288 ±21.5
Contractility index (mmHg/sec.)	469.0 ±78.8	451.0 ±90.8	452.2 ±83.9	459.0 ±82.1	461.5 ±81.0

Table (2) : Effect of bleeding (30% of calculated blood volume) on mean arterial blood pressure (mmHg), heart rate (beat/min) and contractility index (mmHg/second) in the non resuscitated group of rats "group 2" (Mean±SD).

	Mean ± SD					
	Before bleeding	after bleeding				
		30 m.	1h.	2h.	3h.	4h.
Mean arterial B.P.(mmHg)	**B** 94.0 ±7.4	**A** 46.8 ±2.8 ***	**A** 45.6 ±2.8 ***	**A** 46.6 ±3.1 ***	**A** 47.8 ±3.8 ***	**A** 49.7 ±5.1 ***
Heart rate beat/minute	**C** 314.0 ±26.75	**D** 271.0 ±24.2 ***	**D** 270.0 ±22.6 ***	**D** 236.0 ±22.7 ***	**D** 278.0 ±17.2 ***	**D** 277.0 ±25.4 ***
Contractility index mmHg/second	**E** 450.5 ±91.1	**F** 212.5 ±25.2 ***	**F** 211.5 ±22.9 ***	**F** 212.0 ±23.2 ***	**F** 215.0 ±21.0 ***	**F** 214.5 ±18.8 ***

Means without common superscript capital letter are significantly different (P< 0.05) for both rows and columns.
*** **P < 0.001** Very highly significant.

Table (3) : Changes (Mean ± SD) in mean arterial blood pressure (mmHg) before and after bleeding and resuscitation with different solutions at different time from starting resuscitation in rats of "groups 3,4,5 and 6"

	Mean ± S.D.							
	Before bleeding	After bleeding	AFTER RESUSCITATION					
			5 Minutes	30	1h.	2h.	3h.	4h.
Ringer's lactate (RL)	**B** 97.6 ±10.8	**C** 46.7 ±7.9	**A** 75.3 ±8.6 ***	**A** 78.2 ±8.2 ***	**A** 78.2 ±9.1 ***	**A** 77.2 ±9.9 ***	**A** 74.9 ±6.5 ***	**A** 75.1 ±8.6 ***
Hypertonic saline 7.5% (HS)	**B** 95.7 ±9.9	**C** 44.5 ±3.5	**B** 93.8 ±8.9 ***	**B** 94.0 ±8.9 ***	**B** 92.0 ±10.2 ***	**B** 90.0 ±1.1 ***	**B** 86.3 ±8.0 ***	**B** 85.0 ±8.3 ***
6% Dextran 70% (DEX)	**B** 99.2 ±12.8	**C** 48.7 ±4.1	**A** 72.4 ±16.2 ***	**A** 73.4 ±12.1 ***	**A** 73.1 ±6.2 ***	**A** 72.5 ±5.5 ***	**A** 71.8 ±6.3 ***	**A** 73.7 ±9.3 ***
Hypertonic saline + dextran (HSD)	**B** 93.5 ±7.6	**C** 44.4 ±3.2	**B** 87.4 ±9.6 ***	**B** 85.9 ±8.7 ***	**B** 85.3 ±9.8 ***	**B** 84.1 ±7.9 ***	**B** 84.2 ±7.9 ***	**B** 83.4 ±10.1 ***

Means without common superscript capital letter are significantly different (P< 0.05) for both rows and columns.

*** **P < 0.001** Very highly significant.

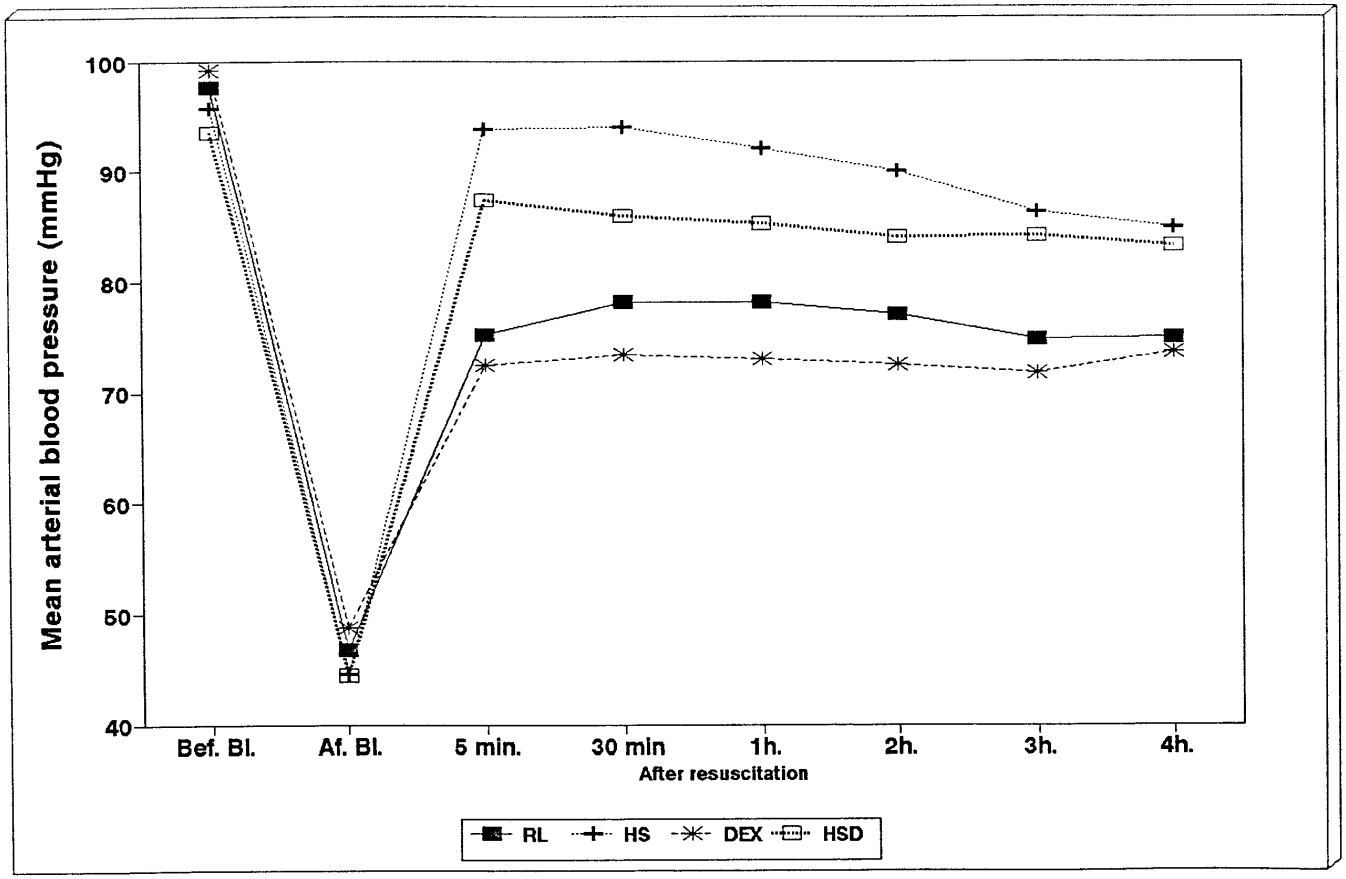
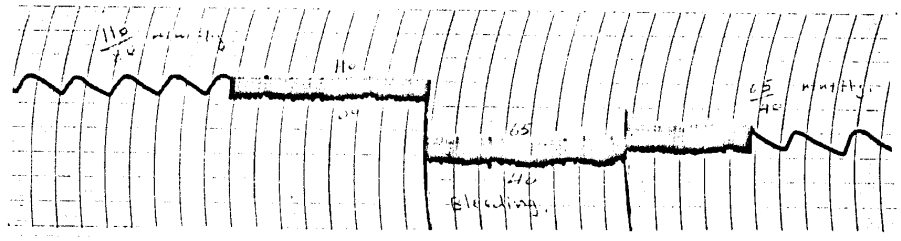
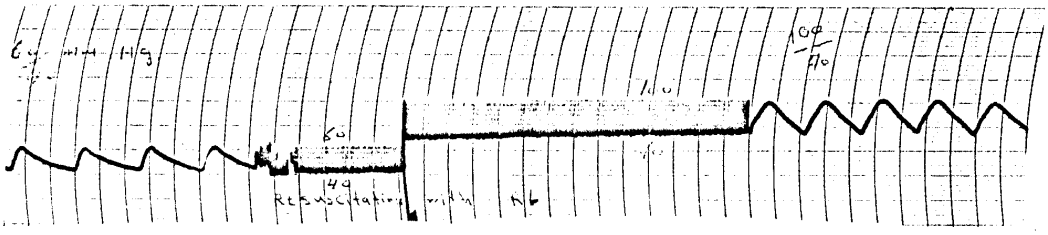


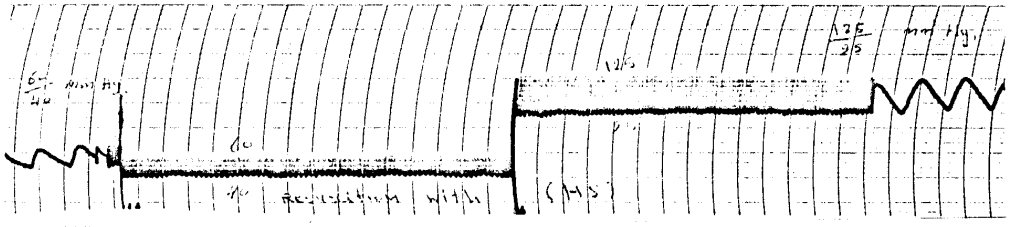
Fig. (9) : Mean values of changes in mean arterial blood pressure (mmHg) before and after bleeding and resuscitation with different solutions at different time from starting resuscitation in rats of groups 3,4,5 & 6.



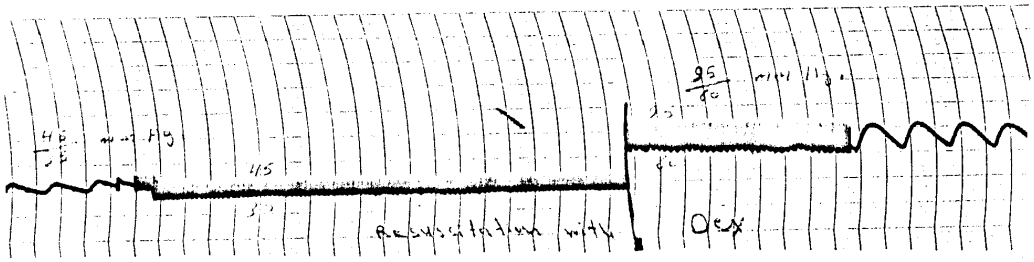
A. Effect of bleeding on blood pressure



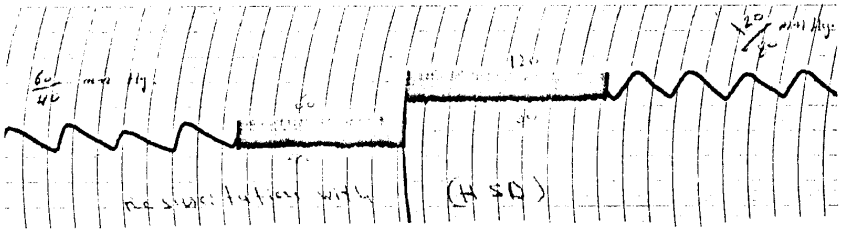
B. Effect of resuscitation with (RL) on blood pressure



C. Effect of resuscitation with (HS) on blood pressure



D. Effect of resuscitation with (Dex) on blood pressure



E. Effect of resuscitation with (HSD) on blood pressure

Fig. (10) : Changes in arterial blood pressure (mmHg) 5 minutes after resuscitation with different solutions in groups 3,4,5 & 6.

Table (4) : Changes (Mean ± SD) in mean heart rate (beat/minute) before and after bleeding and treatment with different resuscitating solutions at different time from starting resuscitation in rats of groups 3,4,5 & 6.

	Mean ± S.D.							
	Before bleeding	After bleeding	AFTER RESUSCITATION					
			5 Minutes	30	1h.	2h.	3h.	4h.
Ringer's lactate (RL)	**B** 314.0 ±37.8	**C** 262.0 ±42.6	**C** 259.0 ±40.0	**A** 278.0 ±42.1 *	**A** 279.0 ±38.1 *	**A** 286.0 ±39.5 **	**A** 280.0 ±34.9 *	**A** 280.0 ±37.4 *
Hypertonic saline 7.5% (HS)	**B** 315.0 ±37.2	**C** 268.0 ±41.3	**A** 279.0 ±42.3 *	**A** 283.0 ±42.2 **	**A** 288.0 ±44.7 **	**A** 292.0 ±39.7 **	**A** 283.0 ±41.4 **	**A** 295.0 ±40.6 ***
6% Dextran 70% (DEX)	**B** 314.0 ±37.5	**C** 255.0 ±37.5	**A** 272.0 ±34.3 ***	**A** 294.0 ±36.9 ***	**A** 283.0 ±34.0 ***	**A** 286.0 ±37.2 ***	**A** 287.0 ±37.7 ***	**A** 290.0 ±37.1 ***
Hypertonic saline + dextran (HSD)	**B** 318.0 ±39.1	**C** 260.0 ±42.4	**A** 265.0 ±40.6	**A** 277.0 ±39.7 **	**A** 280.0 ±44.9 **	**A** 281.0 ±40.1 **	**A** 283.0 ±42.9 **	**A** 280.0 ±41.9 ***

Means without common superscript capital letter are significantly different (P< 0.05) for both rows and columns.

* P < 0.05 Significant

** P < 0.01 Highly significant

*** P < 0.001 Very highly significant

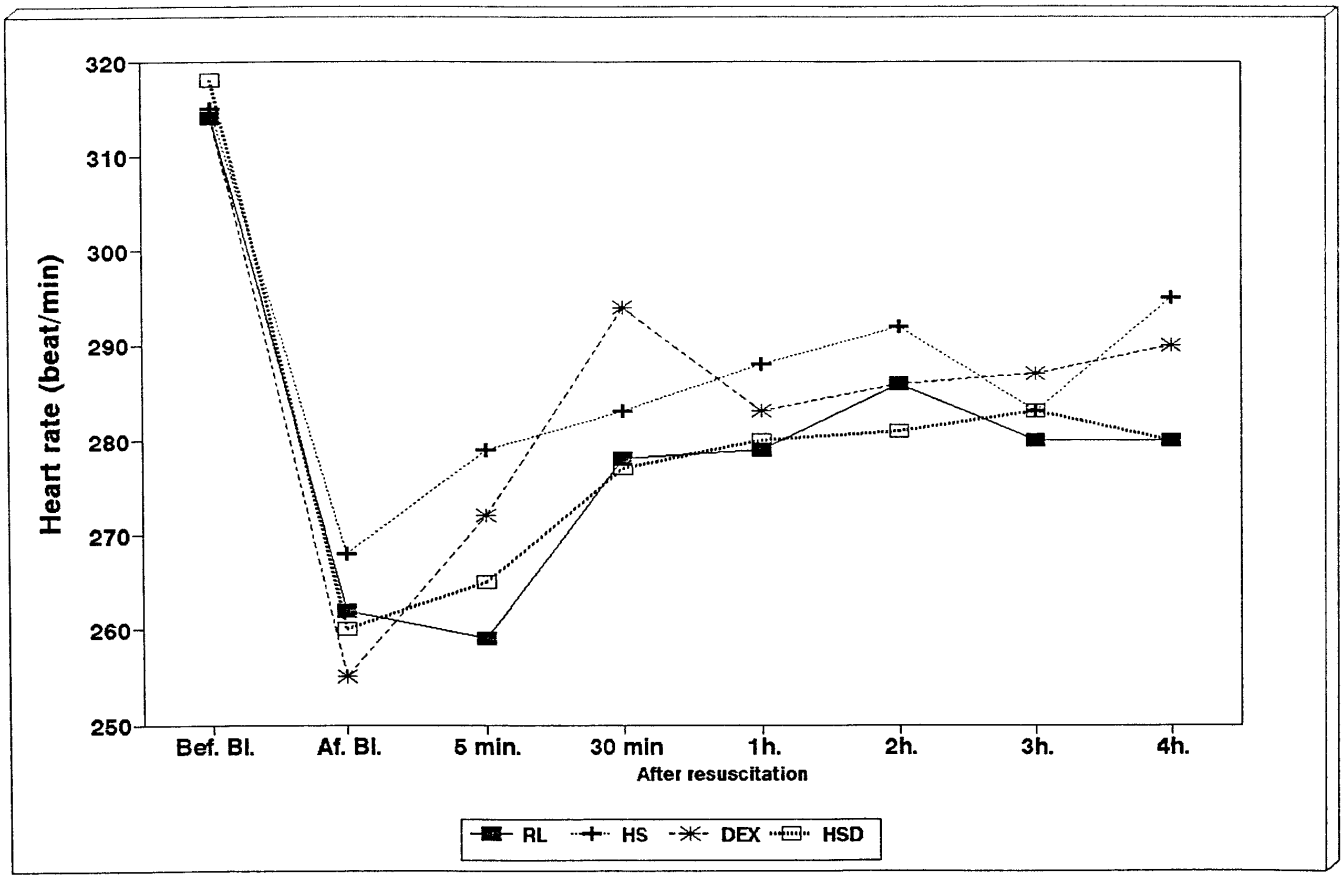


Fig. (11) : Mean values of changes in hart rate (beat/minute) before and after bleeding and resuscitation with different solutions at different time from starting resuscitation in rats of groups 3,4,5 & 6.

Table (5) : Change (Mean ± SD) in mean contractility index (mmHg/second) before and after bleeding and resuscitation with different resuscitation solutions at different time from starting resuscitation in rats of groups 3,4,5 & 6.

	Mean ± S.D.							
	Before bleeding	After bleeding	AFTER RESUSCITATION					
			5 Minutes	30	1h.	2h.	3h.	4h.
Ringer's lactate (RL)	**B** 497.0 ±93.5	**A** 195.0 ±34.3	**C** 309.5 ±68.7 **	**C** 318.0 ±62.9 **	**C** 318.5 ±71.1 **	**C** 319.5 ±69.1 **	**C** 315.0 ±62.0 **	**C** 314.5 ±58.9 **
Hypertonic saline 7.5% (HS)	**B** 487.0 ±81.1	**A** 179.0 ±20.7	**B** 449.5 ±79.4 ***	**B** 452.5 ±81.8 ***	**B** 449.0 ±85.9 ***	**B** 443.5 ±84.2 ***	**B** 439.5 ±86.7 ***	**B** 436.5 ±83.9 ***
6% Dextran 70% (DEX)	**B** 531.0 ±98.9	**A** 201.5 ±15.8	**C** 269.5 ±96.4 **	**C** 299.0 ±79.2 **	**C** 294.0 ±79.2 **	**C** 303.0 ±72.8 **	**C** 302.5 ±72.6 **	**C** 311.0 ±70.9 **
Hypertonic saline + dextran (HSD)	**B** 492.0 ±108.7	**A** 194.0 ±15.9	**B** 431.0 ±102.1 ***	**B** 435.5 ±105.9 ***	**B** 435.5 ±105.9 ***	**B** 428.0 ±99.4 ***	**B** 428.5 ±101.7 ***	**B** 428.5 ±102.7 ***

Means without common superscript capital letter are significantly different (P< 0.05) for both rows and columns.

* P < 0.05 Significant

** P < 0.01 Highly significant

*** P < 0.001 Very highly significant

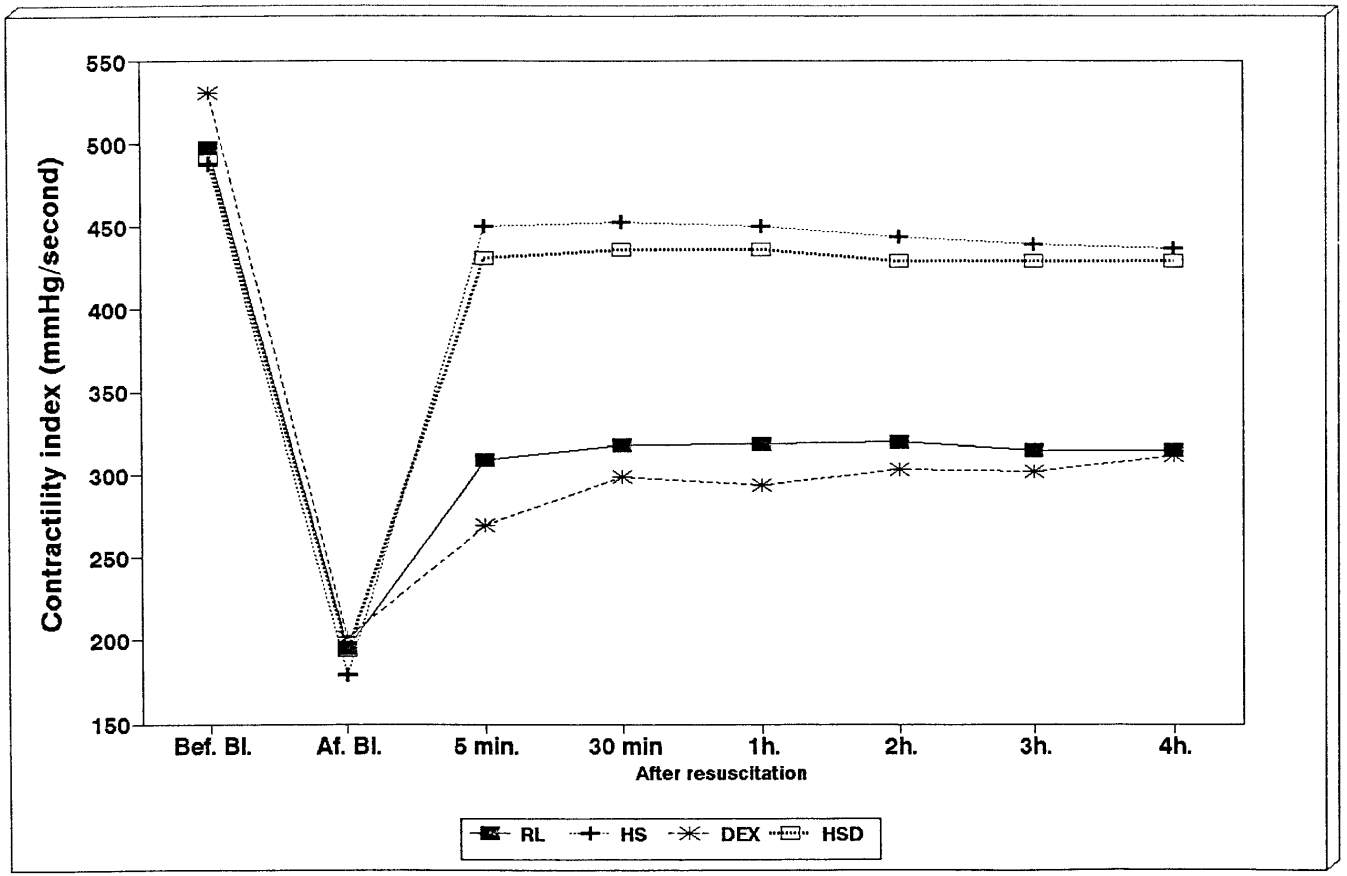


Fig. (12) : Mean values of changes in contractility index (mmHg/second) before and after bleeding and resuscitation with different solutions at different time from starting resuscitation in rats of groups 3,4,5 & 6.

Table (6) : Changes (Mean ± SD) in blood gases (PH, $PaCO_2$, PaO_2) and HCO_3 in response to anaesthesia.

	Mean ± SD	
	Before	After
PH	**A** 7.37 ±0.04	**A** 7.35 ±0.03
$P_a Co_2$ (mmHg)	**B** 40.1 ± 2.0	**B** 39.7 ±16
$P_a O_2$ (mmHg)	**C** 98.8 ±4.5	**C** 98.9 ±4.4
HCo_3 (mmol/L)	**D** 22.4 ±1.9	**D** 22.6 ±1.8

Means without common superscript capital letter are significantly different ($P< 0.05$) for both rows and columns.

Table (7) : Changes (Mean ± SD) in blood gases and bicarbonate before and 4 hours after haemorrhage. in rats of the non resuscitated group (Mean ± SD).

	Mean ± SD	
	Before	After
PH	**A** 7.34 ± 0.03	**E** 7.14 ±0.02 ***
$P_a Co_2$ (mmHg)	**B** 41.2 ± 3.5	**F** 33.8±2.8 ***
$P_a O_2$ (mmHg)	**C** 98.1 ± 2.9	**G** 102.9 ± 4.8 *
HCo_3 (mmol/L)	**D** 22.2 ±2.4	**H** 13.4 ± 1.5 ***

Means without common superscript capital letter are significantly different (P< 0.05) for both rows and columns.

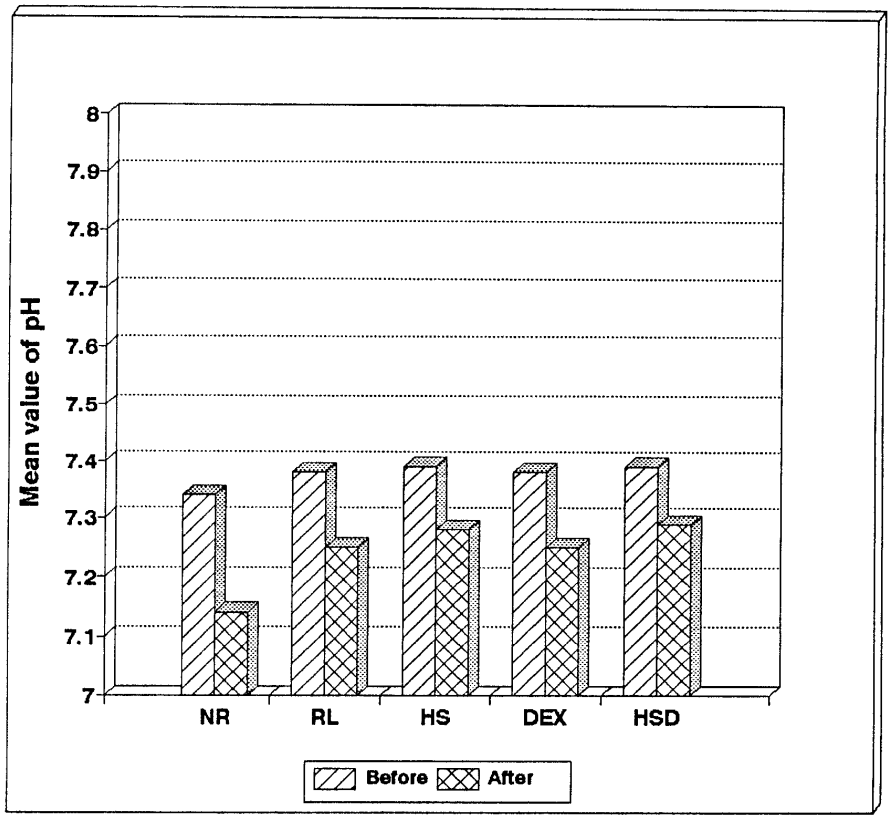
*	P < 0.05	Significant
**	P < 0.01	Highly significant
***	P < 0.001	Very highly significant

Table (8) : Changes (Mean ± SD) in PH before bleeding and 4 hours after resuscitation with different solutions in rats of groups 3,4,5 & 6.

	Mean ± S.D	
	Before	After
Ringer's lactate (RL)	**B** 7.38 ±0.04	**C** 7.25 ±0.04 **
Hypertonic saline 7.5% (HS)	**B** 7.39 ±0.04	**A** 7.28 ±0.04 *
6% Dextran 70% (DEX)	**B** 7.38 ±0.03	**C** 7.25 ±0.04 **
Hypertonic saline + dextran (HSD)	**B** 7.39 ±0.02	**A** 7.29 ±0.02 *

Means without common superscript capital letter are significantly different (P< 0.05) for both rows and columns.

* P < 0.05 Significant
** P < 0.01 Highly significant



NR : Not resuscitated group (control)
RL : Ringer's lactate
HS : Hypertonic saline NaCl 7.5%
DEX : 6% Dextran 70%
HSD : Hypertonic saline + dextran

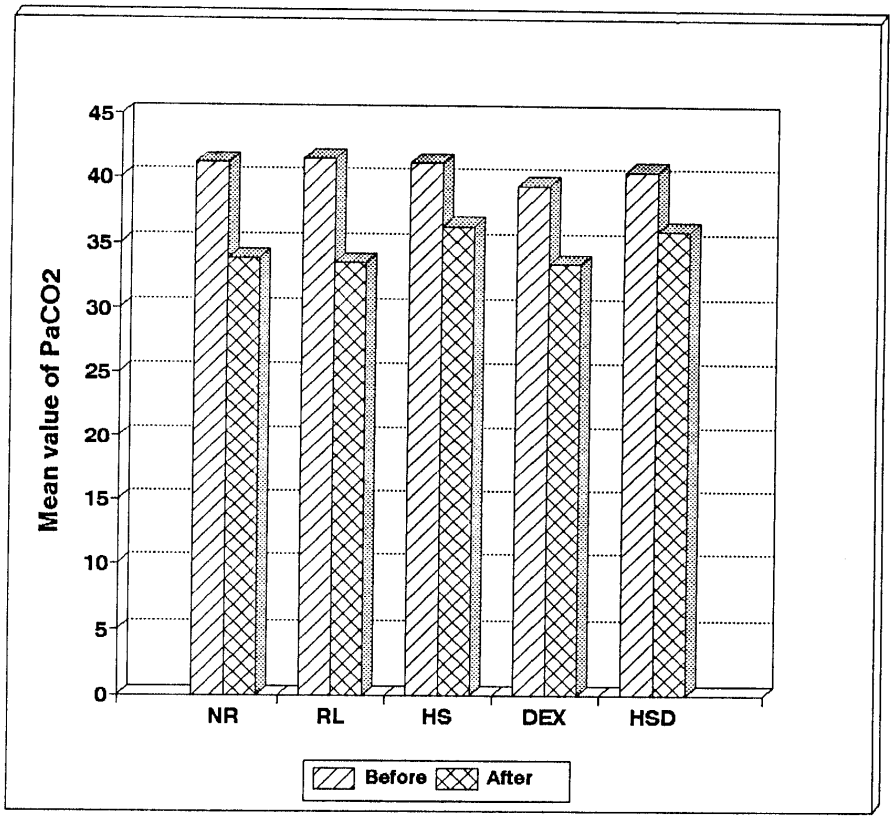
Fig. (13) : Mean values of changes in pH before bleeding and 4 hours after resuscitation with different solutions.

Table (9) : Change (Mean ± SD) in P_aCO_2 (mmHg) before bleeding and 4 hours after resuscitation with different resuscitating solutions in rats of groups 3,4,5 & 5.

	Mean ± S.D	
	Before	After
Ringer's lactate (RL)	**B** 41.5 ±2.4	**C** 33.5 ±2.2 ***
Hypertonic saline 7.5% (HS)	**B** 41.2 ±3.2	**A** 36.3 ±3.5 ***
6% Dextran 70% (DEX)	**B** 39.4 ±1.8	**C** 33.4 ±2.0 ***
Hypertonic saline + dextran (HSD)	**B** 40.5 ±2.8	**A** 36.0 ±2.7 ***

Means without common superscript capital letter are significantly different ($P< 0.05$) for both rows and columns.

*** $P < 0.001$ Very highly significant



NR : Not resuscitated group (control)
RL : Ringer's lactate
HS : Hypertonic saline NaCl 7.5%
DEX : 6% Dextran 70%
HSD : Hypertonic saline + dextran

Fig. (14) : Mean values of changes in PaCO2 before bleeding and 4 hours after resuscitation with different solutions.

Table (10) : Changes (Mean ± SD) in P_aO_2 (mmHg) before bleeding and 4 hours after resuscitation with different resuscitating solutions in rats of groups 3,4,5 & 6.

	Mean ± S.D	
	Before	After
Ringer's lactate (RL)	**B** 98.5 ±4.2	**A** 104.6 ±7.4 *
Hypertonic saline 7.5% (HS)	**B** 104.7 ±8.5	**B** 105.8 ±6.1
6% Dextran 70% (DEX)	**B** 99.6 ±4.6	**A** 104.6 ±7.7 *
Hypertonic saline + dextran (HSD)	**B** 98.5 ±4.96	**B** 101.6 ±5.4

Means without common superscript capital letter are significantly different ($P< 0.05$) for both rows and columns.

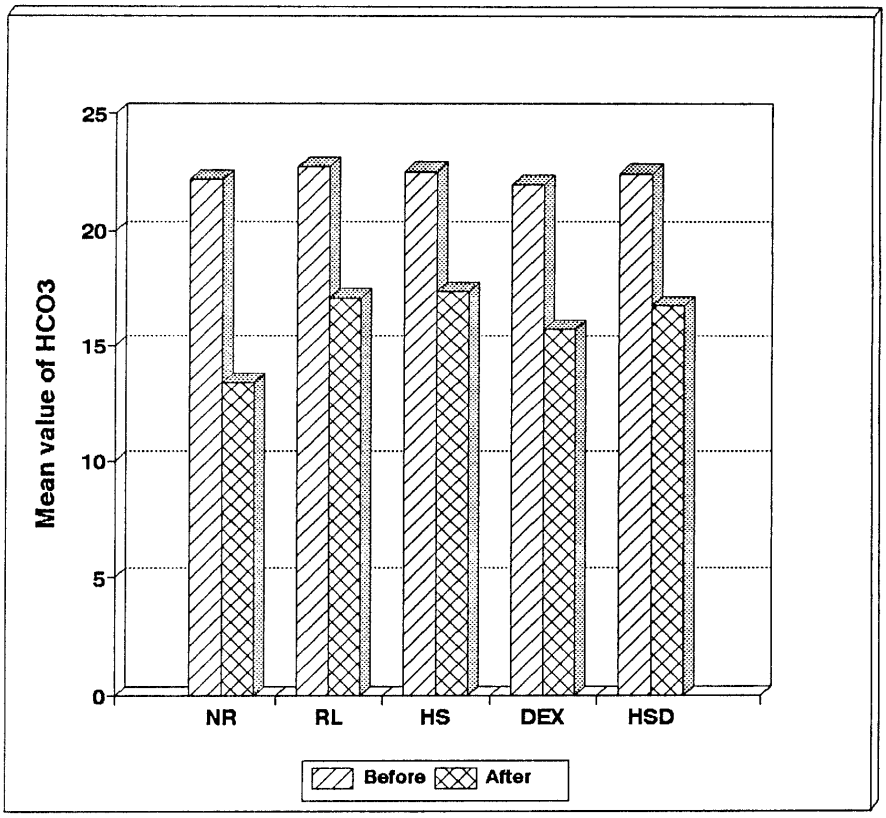
* $P < 0.05$ Significant

Table (11) : Changes (Mean ± SD) in HCo_3 (mmol/L) before bleeding and 4 hours after resuscitation with different solutions in rats of groups 3,4,5 & 6.

	Mean ± S.D	
	Before	After
Ringer's lactate (RL)	**B** 22.7 ±2.1	**A** 17.1 ±1.6 ***
Hypertonic saline 7.5% (HS)	**B** 22.5 ±2.2	**A** 17.4 ±2.6 ***
6% Dextran 70% (DEX)	**B** 21.97 ±2.3	**A** 15.7 ±2.4 ***
Hypertonic saline + dextran (HSD)	**B** 22.4 ±3.1	**A** 16.8 ±2.5 ***

Means without common superscript capital letter are significantly different ($P< 0.05$) for both rows and columns.

*** $P < 0.001$ Very highly significant



NR : Not resuscitated group (control)
RL : Ringer's lactate
HS : Hypertonic saline NaCl 7.5%
DEX : 6% Dextran 70%
HSD : Hypertonic saline + dextran

Fig. (15) : Mean values of changes in HCO3 (mmol/L) before bleeding a 4 hours after resuscitation with different solutions.

Table (12) : Changes (Mean ± SD) in sodium and potassium in (meq/L). just after induction and 4 hours after anaesthesia in sham operated group of rats "group 1".

	Mean ± SD	
	Before	After
Sodium	**B** 139.1 ±3.4	**B** 139.1 ±3.4
Potassium	**A** 3.9 ±0.3	**A** 3.94 ±0.1

Means without common superscript capital letter are significantly different (P< 0.05) for both rows and columns.

Table (13) : Changes (Mean ± SD) in sodium and potassium (meq/L) before and 4 hours after haemorrhage in the rats of non resuscitated groups.

	Mean ± SD	
	Before	After
Sodium	**B** 138.3 ± 3.9	**A** 142.6 ±3.9 ***
Potassium	**C** 3.91 ± 0.4	**D** 4.6 ±0.3 ***

Means without common superscript capital letter are significantly different (P< 0.05) for both rows and columns.

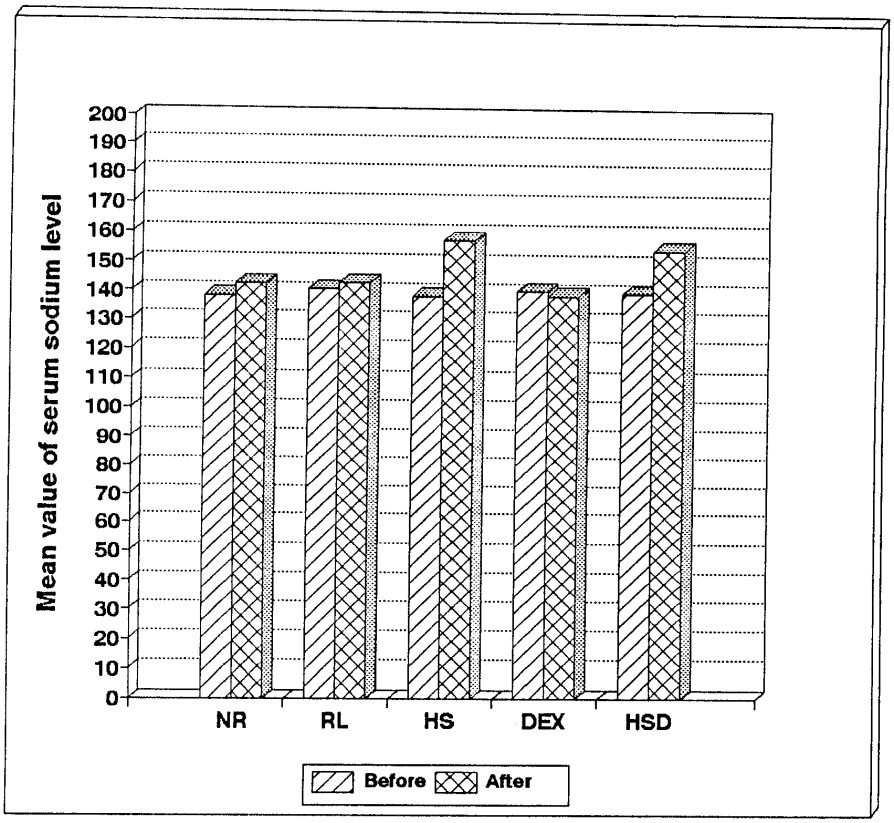
*** P < 0.001 Very highly significant

Table (14) : Changes (Mean ± SD) in serum sodium level (meq/L) before bleeding and 4 hours after resuscitation with different solutions in rats of groups 3,4,5 & 6.

	Mean ± S.D	
	Before	After
Ringer's lactate (RL)	**B** 140.6 ±3.9	**B** 142.7 ±3.2
Hypertonic saline 7.5% (HS)	**B** 138.5 ±2.9	**A** 157.5 ±3.2 ***
6% Dextran 70% (DEX)	**B** 140.3 ±3.3	**B** 138.7 ±3.7
Hypertonic saline + dextran (HSD)	**B** 139.5 ±3.6	**A** 154.4 ±4.4 ***

Means without common superscript capital letter are significantly different (P< 0.05) for both rows and columns.

*** P < 0.001 Very highly significant



NR : Not resuscitated group (control)
RL : Ringer's lactate
HS : Hypertonic saline NaCl 7.5%
DEX : 6% Dextran 70%
HSD : Hypertonic saline + dextran

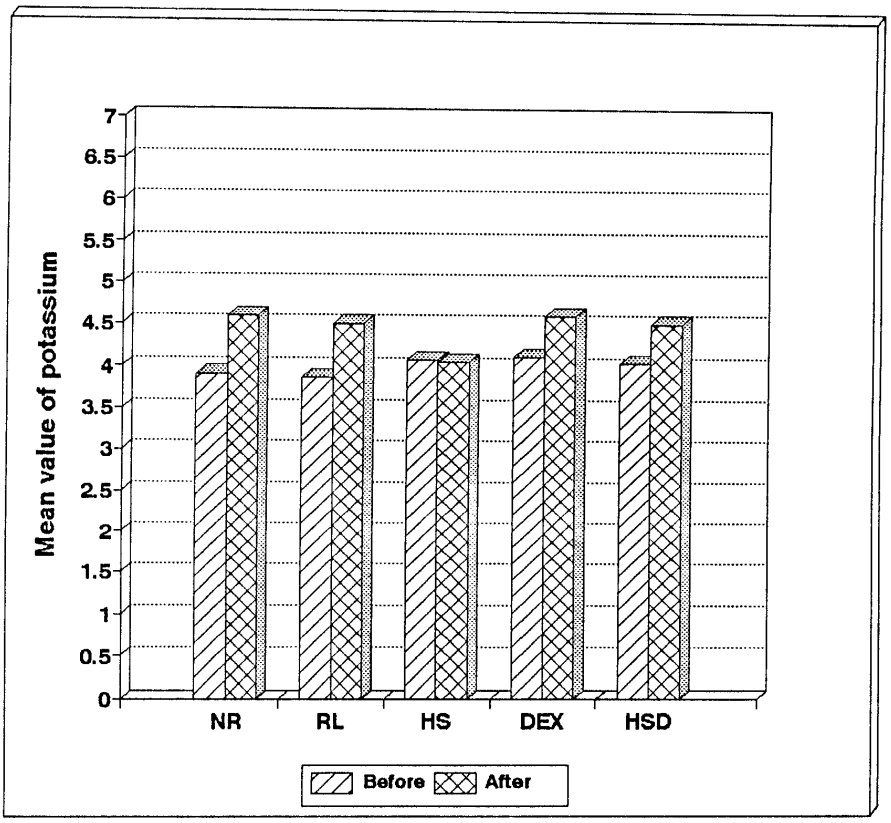
Fig. (16) : Mean value of changes in serum sodium level (mEq/L) before bleeding and 4 hours after resuscitation with different solutions.

Table (15) : Changes (Mean ± SD) in serum level of potassium (meq/l) before and 4 hours after resuscitation with different solutions in rats of groups 3,4,5 & 6.

	Mean ± S.D	
	Before	After
Ringer's lactate (RL)	**B** 3.86 ±0.4	**A** 4.5 ±0.1 *
Hypertonic saline 7.5% (HS)	**B** 4.07 ±0.3	**B** 4.05 ±0.38
6% Dextran 70% (DEX)	**B** 4.11 ±0.5	**A** 4.6 ±0.7 *
Hypertonic saline + dextran (HSD)	**B** 4.03 ±0.4	**A** 4.5 ±0.5 *

Means without common superscript capital letter are significantly different ($P < 0.05$) for both rows and columns.

* $P < 0.05$ Significant



NR : Not resuscitated group (control)
RL : Ringer's lactate
HS : Hypertonic saline NaCl 7.5%
DEX : 6% Dextran 70%
HSD : Hypertonic saline + dextran

Fig. (17) : Mean value of changes in serum level of potassium (mEq/L) bleeding and 4 hours after resuscitation with different solutions.

Table (16) : Changes (Mean ± SD) in hematocrit percentage and mean corpuscular volume (feto liter). Just after induction and 4 hours after anaesthesia in shame operated group of rats "group 1".

	Mean ± SD	
	After induction	4 hours after anesthesia
Hematocrit	**A** 42.2 ±2.3	**A** 41.5 ±2.2
Mean corpuscular volume	**B** 53.6 ±1.8	**B** 53.6 ± 1.6

Means without common superscript capital letter are significantly different (P< 0.05) for both rows and columns.

Table (17) : Changes (Mean ± SD) in hematocrit percentage and mean corpuscular volume (feto-liter) before and 4 hours after bleeding in the non resuscitated group.

	Mean ± SD	
	Before	After
Hematocrit	**B** 43.1 ± 3.2	**A** 34.4 ± 2.3 ***
Mean corpuscular volume	**C** 52.7 ± 1.7	**D** 54.9 ± 1.6 **

Means without common superscript capital letter are significantly different (P< 0.05) for both rows and columns.

** P < 0.01 Highly significant

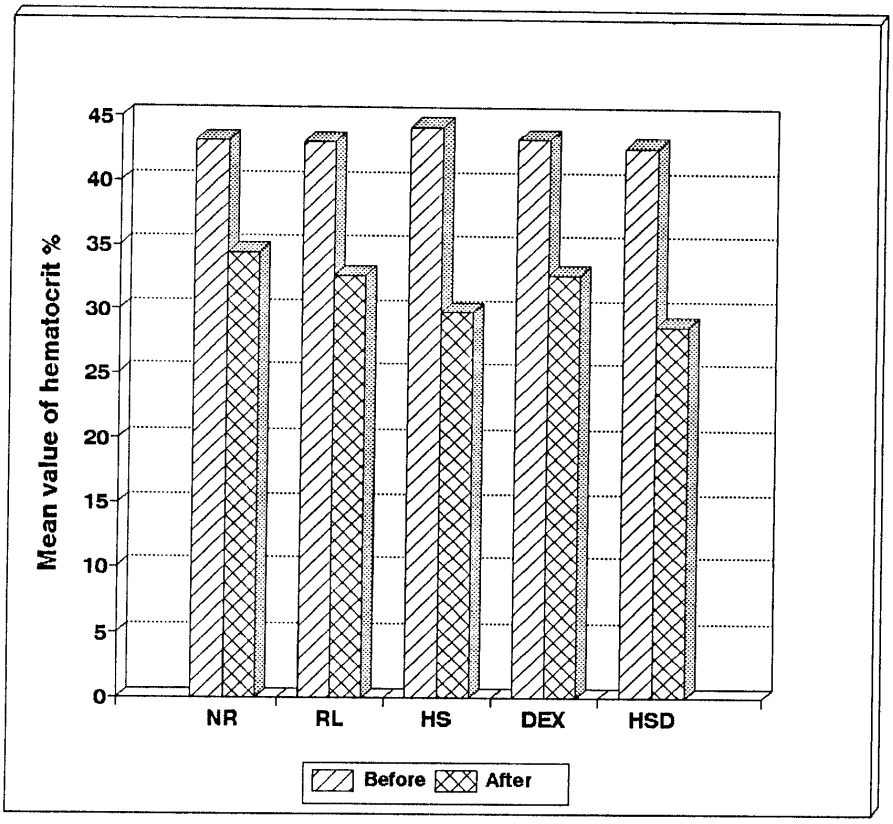
*** P < 0.05 Very highly significant

Table (18) : Changes (Mean ± SD) in hematocrit percentage before bleeding and 4 hours after resuscitation with different solutions in rats of groups 3,4,5 & 6.

	Mean ± S.D	
	Before	After
Ringer's lactate (RL)	**B** 43.0 ±2.9	**A** 32.6 ±2.3 ***
Hypertonic saline 7.5% (HS)	**B** 44.2 ±2.6	**C** 29.8 ±2.9 ***
6% Dextran 70% (DEX)	**B** 43.3 ±2.1	**A** 32.7 ±1.5
Hypertonic saline + dextran (HSD)	**B** 42.7 ±1.1	**C** 28.7 ±2.4 ***

Means without common superscript capital letter are significantly different (P< 0.05) for both rows and columns.

*** P < 0.001 Very highly significant



NR : Not resuscitated group (control)
RL : Ringer's lactate
HS : Hypertonic saline NaCl 7.5%
DEX : 6% Dextran 70%
HSD : Hypertonic saline + dextran

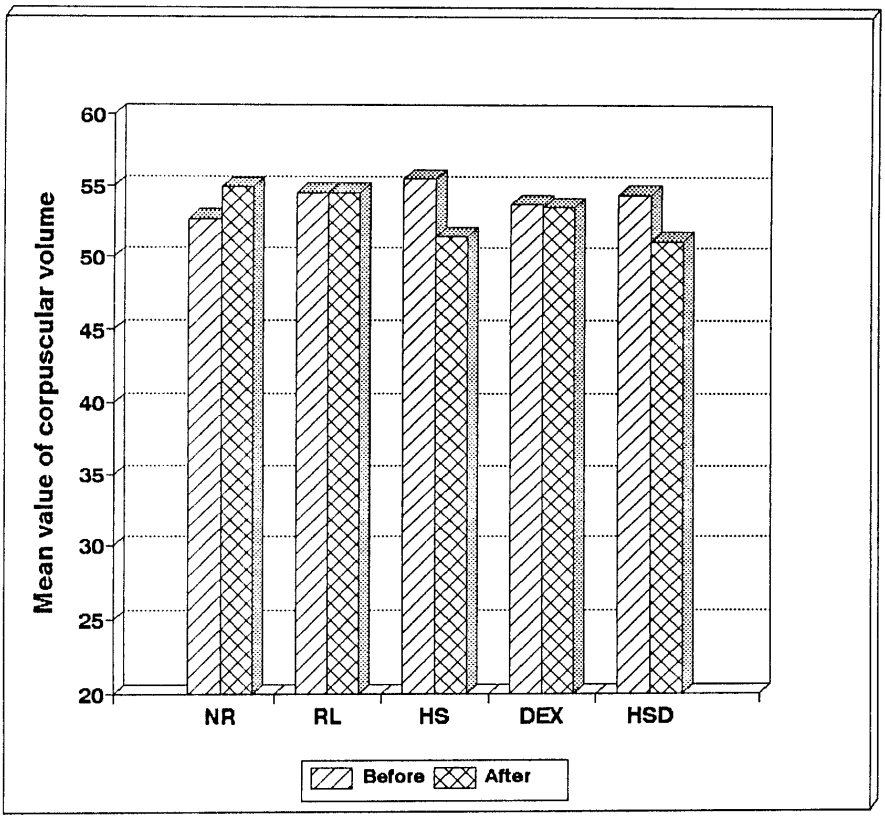
Fig. (18) : Mean values of changes in hematocrit percentage before bleeding and 4 hours after resuscitation with different solutions.

Table (19) : Changes (Mean ± SD) in mean corpuscular volume (in feto liter) before bleeding and 4 hours after resuscitation with different solutions in rats of groups 3,4,5 & 6.

	Mean ± S.D	
	Before	After
Ringer's lactate (RL)	**B** 54.5 ±2.3	**B** 54.5 ±2.4
Hypertonic saline 7.5% (HS)	**B** 55.5 ±1.5	**A** 51.4 ±1.5 ***
6% Dextran 70% (DEX)	**B** 53.7 ±1.2	**B** 53.5 ±1.1
Hypertonic saline + dextran (HSD)	**B** 54.4 ±1.8	**A** 51.1 ±1.5 ***

Means without common superscript capital letter are significantly different (P< 0.05) for both rows and columns.

*** P < 0.001 Very highly significant.



NR : Not resuscitated group (control)
RL : Ringer's lactate
HS : Hypertonic saline NaCl 7.5%
DEX : 6% Dextran 70%
HSD : Hypertonic saline + dextran

Fig. (19) : Mean values of mean corpuscular volume (in feto liter) before bleeding and 4 hours after resuscitation with different solutions.

DISCUSSION

The majority of the early deaths following trauma is attributed to injuries that cause severe blood loss, and those injuries are considered treatable if prompt definitive care is administered **(Dubick and Wade, 1994)**. In the present study, sheding of 30% of the calculated blood volume in rats produced significant decrease in the mean arterial blood pressure (MAP), myocardial contractility (as indicated by the contractility index), and the heart rate, in agreement with the study done by **Wade et al. (1989)** who found that haemorrhage reduced the cardiac index, stroke volume, and mean arterial blood pressure in dogs. Also, **Gross et al. (1990)** found that bleeding in rats was associated with decrease in the mean arterial blood pressure and heart rate. These changes are attributed to the decrease in the blood volume, venous return and the depressant effect of metabolic acidosis on the myocardium.

In the present study it was found that resuscitation of shocked rats with Ringer lactate (RL) solution in volume equal to 3 time the amount

of sheded blood or hypertonic saline 7.5% (HS), 6% dextran 70 (Dex), and a combination of hypertonic saline 7.5% and 6% dextran 70 (HSD) in volume about 1/7 of the volume of sheded blood, produced significant increases in the mean arterial blood pressure, myocardial contractility and heart rate. In fact, in contrast to Ringer lactate and Dextran resuscitation, hypertonic saline (HS) and the hypertonic saline dextran (HSD) mixture have restored these parameters to near normal rapidly within 5 minutes, and could maintain this normality all over the 4 hours which is the time of the experiment. This correlates with the results detected by **Stanford et al. (1989)** who reported that resuscitation of severe haemorrhagic shock, in a porcine model, using hypertonic saline 7.5% (HS) produced more rapid rise in mean arterial blood pressure, over the first ten minutes of resuscitation and more significant increase in cardiac index and urine output than resuscitation by Ringer lactate (RL). Also, the results of the present study are in agreement with those of **Riou and Carli (1990)** who found that hypertonic saline 7.5% (HS) was more effective than isotonic solutions in treating the controlled haemorrhage.

Furthermore, the results of the present work are in agreement with those of **Holcroft et al. (1987)** in clinical resuscitation of trauma

victemes reporting that hypertonic saline dextran (HSD) solution was superior to Ringer lactate (RL) and other crystalloids.

In the other hand, **Mckrinan (1994)** stated that hypertonic saline dextran (HSD) and Ringer lactate (RL) elicited similar heart rate, cardiac output, mean arterial pressure and oxygen transport in the recovery period following haemorrhage and resuscitation. However, this author's work was done on dehydrated pigs, and this may interfere with the mechanism of action of the hypertonic solution.

In the present study, there was no significant difference between the effect of hypertonic saline 7.5% (HS) alone and hypertonic saline in combination with dextran 70 (HSD) on the mean arterial blood pressure (MAP), contractility index and heart rate, in the post resuscitation period throughout the time of the experiment. This correlates with the work done by **Velasco et al. (1980)** who found that hypertonic saline 7.5% (HS) in a dose of 4 ml/kg (equivalent to 10% of the shed blood) given to lightly anaesthetized dogs in severe haemorrhagic shock induced complete and permanent reversal of shock. Also the results of the present study are in agreement with the work done by **Vasser et al. (1993)** on

prehospital resuscitation of hypotensive trauma patients with either normal saline (NS), hypertonic saline 7.5% (HS) or combination of hypertonic saline 7.5% and 6% dextran 70 (HSD). Those authors reported that hypertonic saline 7.5% (HS) alone significantly improved survival rates in high risk patients and the addition of 6% dextran 70 did not offer any additional benefit.

However, the results of the present work are partially in contrast to the study of **Wade et al. (1989)** in their comparative study of resuscitation of conscious pigs following haemorrhagic shock, as they found that hypertonic saline dextran (HSD) was superior to hypertonic saline (HS) and normal saline in restoring mean arterial pressure (MAP) cardiac index (CI) and stroke volume (SV). The discrepancy in the results may be attributed to the difference in the volumes and concentrations of the solutions used together with inconsistency of the time of resuscitation, the degree of shock and the animal model used for the experiment.

The rapid and dramatic effect of hypertonic saline solutions on the mean arterial blood pressure and myocardial contractility was attributed

to plasma volume expansion produced by osmotic fluid shift into the intravascular compartment from intra and extracellular fluid reservoirs (**Gross et al., 1990 and Mckirnan et al., 1994**), as hypertonic saline solutions produced hypernatraemia and hyperosomolarity **(Riou and Carli, 1990).** Also due to non specific precapillary vasodilation of renal, coronary and splanchnic vessels (**Kremeier et al., 1990**) arterial and venous vasoconstriction in muscle and skin due to vagal reflex set off by the lung osmoreceptors **(Riou and Carl, 1990).** Reflex excitation of the sympathetic nervous system could account for the constriction of venules and large arterioles, while a direct effect of hyperosomlarity could explain the dilatation of the smaller arterioles (**Bouskela et al., 1990**).

One of the most important factors, in the restoration of the haemodynamics by infusion of hypertonic saline solutions is the increase in the left ventricular contractility (**Wolf et al., 1971**) due to direct effect of hyperosmolarity and hypernatraemia (**Haim et al., 1992**), increasing myocardial availability of calcium (**Kreimeier et al., 1991**). Increasing concentration of plasma sodium concentration has a positive inotropic effect at an osmolality range of 240 - 320 m.osmol, whereas higher concentrations of sodium has a negative inotropic effect (**Kreimier et al.,**

1993). In addition reflex vagal mechanism provoked by passage of hyperosmolar solutions through the lung may play a role **(Lopes et al., 1981).**

Regarding the effect of haemorrhagic shock and resuscitation on the metabolic state and oxygenation, in the present study showed that, controlled haemorrhagic shock in rats produced significant decrease in arterial blood pH and plasma bicarbonate concentration (metabolic acidosis) and arterial carbon dioxide tension (hyperventilation) and increase in the arterial oxygen tension when these parameters were measured four hours after bleeding. These results go in hormony with the results of **Hannon et al. (1990)**, working on pigs subjected to fixed volume hemorrhage (37.5% ml/kg over one hour), who found that haemorrhage led to increase in arterial PaO_2, haemoglobin saturation, plasma lactate, base deficit, and led to decrease in $PaCO_2$, plasma bicarbonate and arterial pH. These changes were attributed to reduced oxygen delivery, lactacidemia, hyperventilation and haemodilution.

Regarding the effect of resuscitation with different solutions, the present study showed more improvement in the blood pH, with decrease

in the compensatory hyperventilation (increase in $PaCO_2$) when using hypertonic saline solutions (HS) and hypertonic saline dextran (HSD) than when Ringer's lactate (RL) or dextran (Dex) were used. These results correlate with those of **Velasco et al. (1980)** in their comparative study on resuscitation of severe haemorrhage in dogs with either hypertonic saline 7.5% (HS) or normal saline 0.9% (NS), as they detected that resuscitation with hypertonic saline 7.5% (HS) produced gradual rise of $PaCO_2$ (decreased hyperventilation) and that blood pH began to recover towards normal, with improvement of base excess (- 4.8 mEq) at 6 hours post-resuscitation. **Hannon et al. (1990)** stated that during resuscitation of haemorrhagic shock with hypertonic saline dextran (HSD), over 4 hours most cardiopulmonary and metabolic variables (pH, $PaCO_2$, plasma bicarbonate) gradually reversed toward the control level. Thereby ameliorating the deleterious blood gases and acid-base disturbances produced by severe shock.

In contrast to the results of the present study **Mattox et al. (1991)** found that metabolic dranagements associated with trauma (altered pH, Bicarbonate concentration, blood gases) were equally corrected by combination of hypertonic saline dextran and Ringer's lactate and ringer's

lactate alone, when these parameters were measured up on admission to the emergency room. However, the present studies shows results in experimental rats and not in humans.

In the present study, it was found that both hypertonic saline 7.5% (H.S) and combination of hypertonic saline with dextran was equally effective in improving the metabolic state of the shocked rats. This improvement was attributed to the haemodynamic improvement associated with use of hypertonic solutions in resuscitation of haemorrhagic shock **(Vasser et al., 1991).**

Regarding the effect of hypertonic resuscitation on the plasma sodium concentration in shocked rats, in the present study, it was found that hypertonic saline 7.5% (HS) and hypertonic saline dextran (HSD) produced highly significant increase in the plasma sodium concentration while Ringer's lactate (RL) and dextran (Dex) alone produced non significant changes. **Velasco et al. (1987)** found that infusion of hypertonic saline dextran (HSD) at 4 ml/kg resulted in elevations up to 12 mEq/L (15 mEq/L in the present work) in plasma sodium concentration in the experimental animals. Also, **Shackford et al. (1988)**

found that resuscitation of haemorrhagic shock in a procine model using hypertonic saline 7.5% (HS), produced a significant increase in serum sodium and osmolality which resolved within 48 hours. Also, they recorded that hypernatraemia and hyperosmolarity were not associated with renal, or cerebral dysfunction and were corrected through increased sodium excresion and free water intake. Also, in a controlled clinical study in trauma patients, **Vassar et al. (1992)** found that mean serum sodium concentration was 9 mEq/L higher in the treatment group receiving hypertonic saline dextran (HSD) than in the control group receiving Ringer's lactate (RL). They reported that severe hypernatraemia (> 160 mEq/L) occurred in two patients out of 55 without neurological manifestations.

In the present study, comparison of the effect of rescitation with hypertonic saline 7.5% (HS) to hypertonic saline dextran (HSD) on plasma sodium concentration, revealed no significant difference between them. These results are in hormony with that of **Wade et al. (1989)** who found equal increases in plasma sodium concentration and osmolality with hypertonic saline 7.5% (HS) and hypertonic saline dextran (HSD) when used for resuscitation of hemorrhagic shock in conscious pigs.

The increase in plasma sodium concentration during resuscitation with the hypertonic saline solutions is attributed to the high sodium load 2400 ml osmol/liter "1200 mEq/L" **(Trentz and Fredl, 1992)** which is responsible for the rapid improvement of the impaired haemodynamics in controlled haemorrhagic shock **(Gross et al., 1990)**, due to intravascular shift of fluids from the extravascular and intracellular reservoir **(Vencent, 1991)**, and increased myocardial contractility **(Wildenthal et al., 1969)**.

Regarding the effect of resuscitation with the different solutions on the serum potassium level it was found that there was statistically significant increase, when Ringer's lactate (RL), hypertonic saline dextran (HSD) and dextran (Dex) alone were used. However, this change in potassium level was within the clinical range as the maximum recorded mean level was 4.6 mEq/Liter. This increase in potassium level was recorded in the non resuscitated group, so this changes mayb e attributed to the induced haemorrhagic shock and not due to the use of the resuscitating solutions.

Regarding the effect of haemorrhage and resuscitation with hypertonic solutions on the blood haematocrit in rats, in the present study it was found that, controlled haemorrhage (30% of the calculated blood volume) produced significant decrease in the haematocrite value. This result agrees with that of **Mazzoni et al. (1988)** who found a mean hematocrite decrease of 15% after 20% loss of calculated blood volume in rabbits. The decrease in hematocrit in response to blood loss was explained by fluid influx (transcapillary refill) due to the reduction in the capillary pressure produced by bleeding.

In the present study resuscitation of the controlled haemorrhagic shock in rats with hypertonic saline 5% (HS) and hypertonic saline dextran (HSD) produced more significant decrease in hematocrit when compared to the effect of resuscitation with Ringer's lactate (RL) or dextran 70 used alone.

This result is in harmony with that of **Velasco et al. (1980)** who found that a more decrease in the arterial hematocrit with hypertonic saline 7.5% (HS) than with isotonic saline when both was used for resuscitation of haemorrhagic shock in dogs.

The marked decrease in the hematocrit with smaller doses (1/7 volume of sheded blood) of hypertonic saline 7.5% (HS) and combination of hypertonic saline and dextran (HSD), reflects the mobilization of fluids from the extravascular to the intravascular compartment leading to restoration of plasma volume and improvement of the hemodynamics (**Smith et al., 1985**), as hypertonic saline 7.5% (HS) enhances transcapillary refill (**Prist et al., 1994**) due to sudden hypertonic state of the plasma induced by both high salt concentration and the short infusion time (**Mazzoni et al., 1988**).

In the present study, comparison between the effect of hypertonic saline 7.5% (HS) and hypertonic saline dextran (HSD) on plasma volume (as indicated by the arterial hematocrit) revealed no significant difference between them. This is in agreement with **Vasser et al. (1993)** who stated that the addition of 6% dextran 70 to the hypertonic saline 7.5% did not offer any additional benefit. However, **Mazzoni et al. (1988)** found that rapid infusion of one-seventh dose of 7.5% NaCl 6% dextran 70 solution after 20% haemorrhage, blood volume expands to 83% of its control value after 30 min compared to 80.4% when no dextran was added to the hypertonic saline. Thus, the addition of 6% dextran 70 to the hypertonic

saline produced more increase in the blood volume by 2.6% in a 70 Kg persons, which is very small change to be detected in rats with small total blood volume 16 ml/200 gm, if experimental results are applicable to humans. Also, the same result was recorded by **Wade et al. (1990)** in his comparative study between the effect of hypertonic saline 7.5% (HS) and hypertonic saline with added dextran 70 (HSD) in resuscitation of shocked swins after induced controlled haemorrhage (37.5 ml/kg over 60 minutes), as they found that (HSD) produced significantly greater plasma volume expansion than (HS) alone (13.6 compared to 9.9 ml/kg).

Regarding the effect of haemorrhage and resuscitation with hypertonic saline solution on the size of red blood cells as indicated by the mean corpuscular volume, the present study, showed that induced haemorrhagic shock in rats, increased the size of the red blood cells (swelling) when measured 4 hours after sheding of 30% of the calculated blood volume. This agrees with **Nakayama et al. (1984)** who detected that tissue cells swell during shock. Recently, **Mazoni et al. (1992)** demonstrated swelling of the capillary endothelial and red blood cells, due to hypoxia and metabolic acidosis produced by haemorrhagic shock.

In the present study, resuscitation with hypertonic saline (HS) and hypertonic saline-dextran (HSD) produced significant decrease in the size of red blood cells (MCV), while Ringer lactate (RL) and dextran 70 produced non significant effect. Similar results were obtained by **Mazzoni et al. (1988)** who demonstrated that during small volume resuscitation with hypertonic solutions, endogenous fluids were mobilized first of all from the microvascular endothelium and the red blood cells. The shrinkage of red blood cells is attributed to mobilization of fluid from inside the red blood cells due to the increase in the plasma osmolality occurring at the end of bolus infusion of 7.5% hypertonic saline solution.

The decrease in the hematocrit, and the shrinkage of the red blood cells with the reduction in the swelling of capillary endothelium, when hypertonic solutions are used for resuscitation may allow easier blood flow in the capillaries with more improvement of tissue perfusion and oxygenation.

SUMMARY AND CONCLUSION

The present study has been designed to investigate the role of the different hypertonic solutions in resuscitation of experimentally induced controlled haemorrhagic shock.

Sixty albino rats of either sex of local strain weighing 180 to 240 gm were included in the study.

The albino rats were divided into 6 equal groups, each containing 10. Controlled haemorrhagic shock was induced by arteriotomy bleeding through a catheter introduced in the carotid artery, 30% of the calculated blood volume (8.0 ml/100 gm) was shedded over 30 seconds, into a heparinized syringe.

The controlled haemorrhage was followed by resuscitation using either Ringer's lactate (RL) 6 ml/100 gm or hypertonic saline NaCl 7.5%

(HS), 6% dextran 70 (Dex) and a combination of hypertonic aline and 6% dextran 70 at a dose of 0,6 ml/100 gm.

All rats used in the present study were left for one hour after cannulation for haemodyanmic stabilization.

Mean arterial blood pressure, heart rate and contractility index were recorded before bleeding, 30 minutes after bleeding, 5 minutes, 30 minutes, 1h, 2h, 3h and 4 h after resuscitation with different solutions.

Sodium and Potassium levels, hematocrit %, mean corpuscular volume, and blood gases were measured before bleeding and 4 hours after resuscitation.

After statistical analysis, the following results have been recorded :

1. Hemodynamics :

There was more significant increase in mean arterial pressure, heart rate and contractility index when hypertonic saline (HS) and hypertonic saline dextran (HSD) were sued for resuscitation than when Ringer's lactate (RL) or 6% dextran 70 were used.

There was no significant difference between the effect of hypertonic saline and hypertonic saline dextran on the formentioned parameter's.

2. Arterial blood gases and pH :

There was more improvement in blood pH, and more decrease in the compensatory hyperventilation as indicated by the $PaCO_2$ when hypertonic saline (HS) and hypertonic saline dextran (HSD) solutions were used than when Ringer's lactate (RL) and dextran 70 (Dex) were used.

There was no significant difference in the level of plasma bicarbonate concentration when different types of the study solutions were used for resuscitation.

3. Plasma sodium and potassium levels :

There was significant increase in the plasma sodium level only when hypertonic saline and hypertonic saline dextran were used for resuscitation.

There was significant increase in the serum potassium level when Ringer's lactate, hypertonic saline Dextran (HSD) and dextran (Dex) solution, while the hypertonic saline (HS) produce non significant changes.

4. Hematocrite :

There was more decrease in the hematocrite value when measured 4 hours after resuscitation with hypertonic saline and hypertonic saline dextran than when Ringer's lactate and dextran alone were used.

5. Size of the red blood cells :

There was significant decrease in the size of the red blood cells when hypertonic saline and hypertonic saline dextran were used. There was no significant difference between the effect of hypertonic saline (HS) and hypertonic saline dextran on the size of red blood cells when used for resuscitation of haemorrhagic shock.

Conclusion :

If the results of the present study carried out on albino rats hold true to human being, the following clinical conclusions may be suggested in :

1. Hypertonic saline solutions (hypertonic saline 7.5% and hypertonic saline 7.5% in combination with dextran 70) are more effective in resuscitation of severe haemorrhagic shock than Ringer lactate and dextran 70 solutions which are routenly used.

2. Hypertonic saline solution 7.5% is as effective as the combination of the hypertonic saline 7.5% and dextran 70 in restoration of the haemodynamics and acid base state which are usually disturbed by the haemorrhagic shock.

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Mean arterial blood pressure in shown operated group of rats (Group 1)

No	Base	1 hrs.	2 hrs.	3 hrs.	4 hrs.
1	93	93	93	92	90
2	97	95	95	95	96
3	110	108	110	108	110
4	92	93	93	93	94
5	98	95	94	93	98
6	96	93	93	93	93
7	99	97	96	96	99
8	101	104	103	103	102
9	96	93	93	91	95
10	98	97	96	95	97

Heart rate in sham operated group of rats (Group 1)

No	Base	1 hrs.	2 hrs.	3 hrs.	4 hrs.
1	270	270	280	270	270
2	310	310	320	320	310
3	280	280	280	270	280
4	260	260	260	260	260
5	290	290	300	290	290
6	280	280	270	270	280
7	300	310	310	310	320
8	280	280	280	280	280
9	270	260	260	260	270
10	320	320	310	310	320

Contractility index in sham operated group of rats (Group 1)

No	Base	1 hrs.	2 hrs.	3 hrs.	4 hrs.
1	420	400	390	410	410
2	450	420	420	420	420
3	660	640	660	660	660
4	430	420	430	425	425
5	460	440	445	440	450
6	440	420	400	400	400
7	510	480	490	500	500
8	375	365	385	390	395
9	430	415	420	425	435
10	515	510	510	520	520

Mean arterial blood pressure in the non resuscitated group of rats (Group 2) "Control group"

No	Base	after bleed.	1 hrs.	2 hrs.	3 hrs.	4 hrs.
1	97	46	48	52	55	60
2	93	49	46	48	49	52
3	105	46	46	49	50	53
4	85	49	46	43	42	43
5	104	50	52	50	51	52
6	94	43	42	44	45	45
7	97	48	44	43	44	44
8	95	44	43	46	48	50
9	87	43	44	45	48	42
10	83	50	45	46	46	50

Hart rate in the non resuscitated group of rats (Group 2) "Control group"

No	Base	after bleed.	1 hrs.	2 hrs.	3 hrs.	4 hrs.
1	280	260	250	260	260	270
2	300	260	260	260	270	260
3	310	240	260	260	280	280
4	360	320	320	330	320	340
5	330	290	290	290	280	280
6	350	280	280	290	290	280
7	310	260	260	260	270	280
8	300	280	270	280	280	270
9	280	240	240	260	260	240
10	320	280	270	270	270	270

Contractility index in the non resuscitated group of rats (Group 2) "Control group"

No	Base	after bleed.	1 hrs.	2 hrs.	3 hrs.	4 hrs.
1	430	215	230	230	225	230
2	410	210	215	215	215	230
3	630	185	190	190	205	205
4	370	200	220	215	215	215
5	590	260	255	265	265	250
6	420	190	195	200	200	210
7	490	220	210	200	210	200
8	400	180	175	185	185	185
9	390	225	225	220	225	220
10	375	240	200	220	210	200

Mean arterial blood pressure in rats of (Group 3)

No.	Base	Aft. ble.	5	30	1 h.	2 h.	3 h.	4 h.
1	105	50	76	77	85	82	82	80
2	110	60	96	97	96	98	93	92
3	83	38	70	73	62	67	68	67
4	115	50	68	70	77	76	70	70
5	97	47	83	87	86	85	83	84
6	86	41	68	74	76	74	74	73
7	92	55	76	78	74	75	73	70
8	87	33	70	72	73	62	64	63
9	104	48	73	74	78	78	76	76
10	97	45	73	76	75	75	76	76

Heart Rate in rats of (Group 3)

No.	Base	Aft. ble.	5	30	1 h.	2 h.	3 h.	4 h.
1	360	320	340	340	330	350	340	350
2	300	220	240	240	240	240	240	240
3	340	280	240	300	300	3000	280	280
4	260	200	220	230	240	240	240	240
5	320	280	280	260	260	270	270	260
6	260	220	230	230	240	260	260	260
7	280	220	240	260	260	270	260	260
8	320	280	270	270	270	270	270	270
9	360	300	320	340	340	240	320	320
10	340	300	310	310	310	320	320	320

Contratility index in rats of (Group 3)

No.	Base	Aft. ble.	5	30	1 h.	2 h.	3 h.	4 h.
1	540	190	410	400	420	400	400	390
2	630	170	440	445	445	460	430	425
3	390	180	230	240	210	220	220	220
4	650	190	330	340	350	350	330	330
5	440	210	280	290	295	290	290	495
6	410	190	295	260	295	290	285	295
7	430	200	300	305	295	295	300	290
8	460	195	255	240	250	260	260	265
9	570	210	295	290	310	315	310	315
10	450	215	310	310	315	315	325	325

Mean arterial blood pressure in rats of (Group 4)

No.	Base	Aft. ble.	5	30	1 h.	2 h.	3 h.	4 h.
1	118	50	116	115	119	107	100	100
2	97	45	98	100	97	93	92	92
3	103	40	93	90	90	93	92	90
4	100	50	93	97	87	83	73	73
5	88	45	90	91	90	89	78	77
6	86	46	86	84	84	83	80	79
7	90	44	93	93	92	93	90	90
8	85	40	83	85	85	85	84	81
9	96	43	96	96	88	88	90	88
10	94	42	90	89	88	86	84	88

Heart Rate in rats of (Group 4)

No.	Base	Aft. ble.	5	30	1 h.	2 h.	3 h.	4 h.
1	360	300	320	320	320	310	330	330
2	340	300	320	320	320	320	320	320
3	380	330	350	350	360	360	360	360
4	290	260	260	270	260	270	280	280
5	270	200	230	230	230	240	240	240
6	280	240	240	230	240	260	250	250
7	320	270	270	280	290	290	280	290
8	280	230	250	250	260	250	250	260
9	360	310	310	320	340	340	340	340
10	290	240	240	260	260	280	280	280

Contractility index in rats of (Group 4)

No.	Base	Aft. ble.	5	30	1 h.	2 h.	3 h.	4 h.
1	680	240	630	640	660	650	650	640
2	440	185	400	410	430	425	425	425
3	375	175	380	375	375	370	360	365
4	420	190	405	415	400	395	380	385
5	390	210	375	375	370	370	360	360
6	410	185	395	395	385	385	390	380
7	440	205	440	440	440	420	420	410
8	520	175	520	525	500	500	500	500
9	515	215	480	480	470	460	460	450
10	480	210	470	770	450	460	450	450

Mean arterial blood pressure in rats of (Grouop 5)

No.	Base	Aft. ble.	5	30	1 h.	2 h.	3 h.	4 h.
1	83	43	65	68	70	70	70	70
2	112	57	117	100	80	80	83	83
3	93	48	60	60	70	73	67	67
4	120	50	70	83	83	77	77	93
5	100	47	70	70	68	68	65	65
6	113	53	69	80	80	80	79	80
7	88	45	67	70	73	73	71	72
8	84	46	63	64	66	64	64	64
9	103	50	75	77	75	74	74	76
10	96	48	62	62	66	66	68	67

Heart Rate in rats of (Group 5)

No.	Base	Aft. ble.	5	30	1 h.	2 h.	3 h.	4 h.
1	340	280	310	320	320	310	320	320
2	280	230	240	260	250	250	260	260
3	360	310	340	340	330	340	340	340
4	280	230	240	240	250	240	240	260
5	320	280	300	310	310	310	300	300
6	220	210	260	250	260	260	260	260
7	310	260	270	280	280	280	280	280
8	320	220	290	280	270	280	290	290
9	380	320	320	320	330	340	340	350
10	270	210	250	240	240	250	240	240

Contractility index in rats of (Group 5)

No.	Base	Aft. ble.	5	30	1 h.	2 h.	3 h.	4 h.
1	400	185	260	260	265	270	275	270
2	630	220	550	510	490	490	490	490
3	460	190	240	240	250	250	260	290
4	660	210	260	270	280	280	270	290
5	580	230	290	290	295	300	300	300
6	620	210	330	340	345	340	340	360
7	450	190	270	280	290	290	290	295
8	410	185	215	225	220	230	230	225
9	610	205	320	320	320	315	310	300
10	490	190	230	230	255	255	260	290

Mean arterial blood pressure in rats of (Group 6)

No.	Base	Aft. ble.	5	30	1 h.	2 h.	3 h.	4 h.
1	103	48	90	90	93	87	90	90
2	97	48	92	92	85	85	85	87
3	93	43	100	87	87	87	86	86
4	86	40	78	76	76	77	73	72
5	105	47	103	103	108	103	107	107
6	84	44	75	75	78	78	74	75
7	98	40	83	83	82	80	80	80
8	86	44	76	76	74	75	76	78
9	97	48	90	90	83	83	87	87
10	86	42	93	87	87	86	84	80

Heart Rate in rats of (Group 6)

No.	Base	Aft. ble.	5	30	1 h.	2 h.	3 h.	4 h.
1	360	280	320	340	340	330	330	340
2	280	230	240	240	230	240	250	250
3	380	280	320	330	350	350	360	350
4	310	280	280	280	290	280	280	290
5	300	230	220	260	270	270	250	250
6	360	310	310	320	320	320	330	320
7	280	220	240	240	230	240	250	250
8	340	300	260	270	280	280	280	280
9	300	240	250	260	260	270	270	260
10	270	230	210	230	230	230	230	230

Contractility index in rats of (Group 6)

No.	Base	Aft. ble.	5	30	1 h.	2 h.	3 h.	4 h.
1	620	220	530	530	540	510	530	530
2	640	185	600	610	600	590	590	595
3	590	195	505	505	515	505	505	505
4	460	210	410	410	514	405	405	400
5	560	175	480	480	490	480	485	485
6	375	190	315	320	320	315	310	300
7	430	205	400	400	410	390	390	390
8	385	170	310	320	300	310	310	310
9	520	205	460	470	470	475	460	460
10	340	185	300	290	295	300	300	310

Values of measured PH before and after bleeding and resurcitation in the different groups of rats.

	Group 1		Group 2		Group 3		Group 4		Group 5		Group 6	
	bef.	Af.	Bef.	Af.	Bef.	Af.	Bef.	Af.	Bef.	Af.	Bef.	Af.
1	7.31	7.31	7.36	7.12	7.34	7.21	7.39	7.28	7.30	7.28	7.39	7.28
2	7.34	7.36	7.35	7.13	7.44	7.25	7.41	7.22	7.38	7.26	7.40	7.31
3	7.39	7.36	7.34	7.16	7.36	7.22	7.41	7.30	7.40	7.24	4.39	7.26
4	7.36	7.33	4.32	7.14	7.34	7.29	7.35	7.28	7.39	7.31	7.36	7.29
5	7.44	7.43	7.38	7.16	7.42	7.31	7.36	7.29	7.38	7.29	7.38	7.28
6	7.34	7.31	7.29	7.10	7.38	7.29	7.42	7.33	7.34	7.28	7.41	7.32
7	7.33	7.34	7.34	7.13	7.43	7.26	7.39	7.28	7.31	7.29	7.40	7.32
8	7.36	7.35	7.31	7.13	7.35	7.29	7.40	7.21	7.41	7.25	7.36	7.28
9	7.41	7.42	7.35	1.14	7.33	7.19	7.36	7.29	7.38	7.27	7.39	7.27
10	7.38	7.37	7.39	7.15	7.36	7.23	7.41	7.31	7.40	7.24	7.38	7.30

Values of the measured $P_a Co_2$ before and after resuscitation in the different groupes of rats.

	Group 1		Group 2		Group 3		Group 4		Group 5		Group 6	
	bef.	Af.	Bef.	Af.	Bef.	Af.	Bef.	Af.	Bef.	Af.	Bef.	Af.
1	41	39	39	29	43	36	43	38	42	35	45	40
2	43	40	45	38	40	37	45	36	38	34	39	35
3	39	38	38	33	41	31	46	40	39	33	39	35
4	38	39	39	34	45	33	38	34	41	36	38	34
5	40	41	48	36	45	35	38	33	38	33	39	36
6	39	38	43	32	39	30	38	34	37	30	40	34
7	40	41	38	33	42	34	42	37	40	36	39	34
8	38	38	44	37	44	34	39	33	39	32	38	33
9	44	41	39	31	38	30	44	37	42	34	45	41
10	39	38	39	35	41	35	39	32	38	31	43	38

Values of measured arterial (P_aO_2) in (mmHg) before and after bleeding and resusictation in different groups of rats.

	Group 1		Group 2		Group 3		Group 4		Group 5		Group 6	
	bef.	Af.	Bef.	Af.	Bef.	Af.	Bef.	Af.	Bef.	Af.	Bef.	Af.
1	96	102	102	112	96	110	104	108	106	118	110	103
2	96	96	98	104	93	103	120	110	98	104	99	96
3	95	95	96	102	102	115	98	103	93	96	94	110
4	102	98	97	101	106	109	116	120	95	93	102	106
5	98	98	99	106	98	96	103	104	98	103	96	104
6	110	110	96	108	104	108	96	108	106	115	94	97
7	97	99	95	98	98	104	94	98	96	108	100	103
8	95	96	96	102	96	106	100	96	102	106	96	98
9	100	98	98	96	98	106	106	108	98	101	99	106
10	99	97	104	100	94	89	110	103	104	102	95	93

Values of meaured HCo_3 (m.mol/L) before and 4 hours after bleeding and resuscitation in different groups of rats

	Group 1		Group 2		Group 3		Group 4		Group 5		Group 6	
	bef.	Af.	Bef.	Af.	Bef.	Af.	Bef.	Af.	Bef.	Af.	Bef.	Af.
1	21.9	21.1	21.8	13.2	22.0	17.0	23.2	17.3	23.0	18.1	21.1	14.4
2	22.3	22.6	20.0	12.3	21.3	16.2	22.3	17.1	24.6	18.6	27.0	19.0
3	22.0	23.0	24.0	14.5	23.1	20.7	22.4	19.7	20.3	18.4	25.2	18.1
4	24.8	24.3	22.0	16.0	23.7	17.8	21.9	19.3	24.0	16.1	23.2	17.3
5	18.3	18.4	21.6	12.3	26.0	16.8	24.0	18.7	23.1	15.2	18.4	11.2
6	21.2	21.8	20.2	13.4	21.0	15.3	22.8	15.8	20.0	14.3	22.3	17.6
7	22.4	23.0	24.3	13.1	24.3	18.1	18.3	13.1	26.2	15.9	25.5	18.9
8	24.0	24.0	26.4	15.4	22.6	16.8	24.0	17.9	20.1	15.8	19.3	14.8
9	23.1	23.2	18.1	11.2	18.3	14.9	26.0	20.3	18.6	13.1	24.0	18.3
10	24.4	24.6	23.3	12.6	23.8	17.6	19.6	15.1	19.8	11.3	18.1	18.4

Values of measured plasma potasium level (mEqu/L) before and after bleeding and resuscitation in the different groups of rats

	Group 1		Group 2		Group 3		Group 4		Group 5		Group 6	
	bef.	Af.	Bef.	Af.	Bef.	Af.	Bef.	Af.	Bef.	Af.	Bef.	Af.
1	3.6	3.9	4.1	4.5	3.7	3.9	3.9	4.2	4.3	4.6	3.8	4.3
2	4.2	4.1	3.6	4.5	3.3	4.0	3.6	3.6	5.1	5.0	4.5	4.9
3	3.5	3.8	3.4	4.3	4.6	5.1	4.1	4.2	3.5	4.1	3.5	3.4
4	4.1	4.1	3.8	4.4	3.7	4.1	4.3	4.6	4.2	4.9	4.2	4.8
5	3.9	3.8	4.3	4.9	4.2	6.3	4.6	4.2	3.4	4.1	3.6	4.3
6	4.3	4.2	4.6	5.4	3.6	4.1	3.8	4.2	4.6	6.1	4.5	5.1
7	3.6	3.8	3.5	4.3	3.9	4.4	4.5	4.4	3.8	4.1	3.9	4.2
8	4.1	3.9	4.1	4.6	3.7	4.2	4.1	4.0	3.6	3.9	4.5	5.1
9	3.9	3.9	3.9	4.6	3.8	4.5	4.0	3.4	4.1	4.8	4.0	4.4
10	3.8	3.9	3.8	4.9	4.1	4.8	3.8	3.7	4.5	4.4	3.8	4.1

Values of measured plasma sodium (mEq/L) concentration before and after resuscitation in different groups of rats

	Group 1		Group 2		Group 3		Group 4		Group 5		Group 6	
	bef.	Af.	Bef.	Af.	Bef.	Af.	Bef.	Af.	Bef.	Af.	Bef.	Af.
1	137	137	146	149	148	145	143	158	143	135	143	158
2	142	141	142	146	145	145	135	163	136	141	135	156
3	136	135	136	141	139	148	140	153	146	138	146	161
4	143	141	135	138	143	144	142	156	142	144	142	151
5	145	146	142	144	136	138	138	163	143	133	136	149
6	138	141	139	146	139	141	136	157	139	142	138	156
7	136	135	135	138	136	138	135	155	136	143	141	159
8	140	140	138	144	141	143	139	158	141	138	140	155
9	139	138	134	138	141	144	141	156	138	135	139	151
10	135	137	136	142	138	141	136	156	139	138	135	148

Values of measured haematocrit % before and after bleeding and resuscitation in different groups of rats

	Group 1		Group 2		Group 3		Group 4		Group 5		Group 6	
	bef.	Af.	Bef.	Af.	Bef.	Af.	Bef.	Af.	Bef.	Af.	Bef.	Af.
1	43.0	43.0	43.6	36.0	46.0	31.0	45.9	31.8	41.5	34.2	47.0	30.1
2	46.0	44.0	42.0	35.0	38.8	32.4	46.2	28.1	46.0	33.0	42.0	24.0
3	39.0	39.0	46.0	36.0	38.1	28.2	43.0	31.5	43.3	34.0	43.0	28.2
4	42.6	42.1	45.0	37.0	43.0	35.0	46.0	28.6	43.0	32.5	41.5	29.3
5	44.0	43.0	47.0	37.0	43.0	34.0	42.0	34.0	45.1	31.2	44.0	31.2
6	44.0	44.0	46.0	34.0	47.0	34.0	47.0	24.3	46.0	34.0	43.0	32.0
7	39.0	38.0	38.0	31.0	42.0	31.0	39.0	31.0	45.0	34.0	42.0	26.0
8	43.0	42.0	44.0	35.0	42.0	32.0	45.0	29.0	44.0	33.0	43.0	29.0
9	41.0	41.0	39.0	32.0	45.0	36.0	42.0	33.0	40.0	31.0	41.0	29.0
10	40.0	39.0	40.0	31.0	45.0	32.0	46.0	27.0	39.0	30.0	40.0	28.0

Values of measured mean corpusular volume before and 4 hours after bleeding and resuscitation in the different groups.

	Group 1		Group 2		Group 3		Group 4		Group 5		Group 6	
	bef.	Af.	Bef.	Af.	Bef.	Af.	Bef.	Af.	Bef.	Af.	Bef.	Af.
1	51.2	52.1	51.9	53.8	50.0	50.0	55.4	52.6	53.1	53.2	56.0	52.0
2	52.8	52.8	50.1	53.8	57.1	57.5	57.3	51.2	52.1	53.4	53.6	50.9
3	53.0	52.0	51.0	54.2	57.5	57.5	53.9	50.1	54.2	54.1	52.0	51.1
4	56.0	56.0	52.0	54.9	53.1	53.2	56	50.3	53.1	53.6	54.6	51.6
5	53.6	53.1	55.1	57.3	56.1	56.0	56.0	52.3	54.4	54.2	53.2	50.1
6	56.3	56.1	53.0	54.0	54.2	53.9	54.0	51.2	53.0	53.1	55.1	51.2
7	51.4	52.0	52.0	53.1	55.1	55.2	57.1	55.0	56.0	56.2	52.0	50.1
8	55.0	55.1	55.3	57.6	51.9	51.6	53.0	50.2	52.4	52.1	56.0	53.7
9	53.8	53.6	52.1	54.6	54.6	54.6	55.4	51.2	53.3	53.6	54.0	51.15
10	52.6	52.8	54.2	56.4	55.1	55.2	56.8	50.3	54.9	54.5	57.3	54.7

THE ROLE OF HYPERTONIC SOLUTIONS IN RESUSCITATION OF HEMORRHAGIC SHOCK IN EXPERIMENTAL ANIMALS

Protocol of
THESIS
Submitted in Partial Fulfillment
for the M.D. Degree
IN
ANAESTHESIOLOGY

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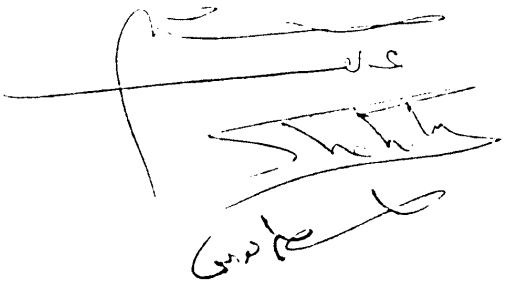
INTRODUCTION

Despite the advances in primary care, trauma in conjunction with shock remains the leading cause of morbidity and mortality specialy in teenagers and young adults **(Kreimeier et al., 1993).**

Pore hospital, preoperative and intensive care related efforts aim to reduce the number of trauma deaths through the improvement of resuscitation from the hypovolaemic shock, and rapid restoration of oxygen delivery to the tissues **(Fleming et al., 1982).**

However, large-volume fluid therapy may fail in resuscitation of hypovolaemic shock, the primary reason appear to be the fact that the volume necessary to compensate for massive blood loss can rarely be adequately replaced during the pre - hospital period **(Kaweski et al., 1990).**

Infusion of small volumes of hypertonic sodium chloride solution has recently been used for the treatment of haemorrhagic shock. An infusion of 7.5% sodium chloride in a volume equal to 10% of the shed blood in dogs successfully restored normal circulatory function and improved survival time without accompanying blood transfusion **(Reuven et al., 1989).**



The value of hypertonic saline solution was interpreted by **Smith et al.** (1985) to be due to increased mean arterial pressure and cardiac output with marked elevation of renal, mesenteric, total splanchnic and coronary blood flow.

AIM OF THE WORK

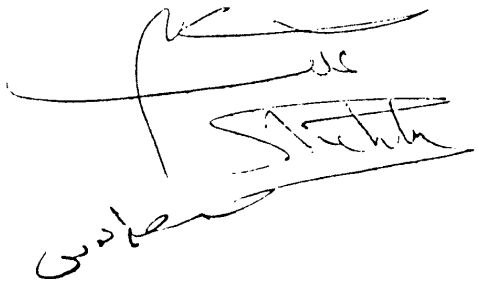
This study is designed to investigate the role of different hypertonic solutions in resuscitation of experimentally induced controlled haemorrhagic shock mainly in albino rats and other experimental animals if needed.

MATERIALS AND METHODS

This controlled experimental study will be carried out on 6 groups of anaesthetized albino rats, controlled bleeding will be ashieved by sheding of about 30% of blood volume, followed by resuscitation using different fluid solutions as following :

Group I : Normal animals :

No bleeding will be induced, for studying the effect of anaesthesia, cannulation and fasting on the animals.



Group II : Control group

The rats will not be resuscitated after the induced bleeding.

Group III :

The rats will be resuscitated using ringer lactate 60 ml/kg over 5 min.

Group IV :

The rats will be resuscitated using NaCl 7.5%, 6 ml/kg over 5 min.

Group V :

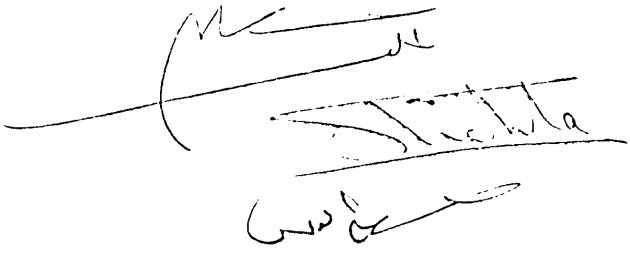
The rats will be resuscitated using 6% dextran 70, 6 ml/kg over 5 min.

Group VI :

The rats will be resuscitated using combination of NaCl% and 6% dextran 70 over 5 min.

<u>The parameters will be studied are :</u>

- **Haemodynamic parameters**
  - Pulse rate.
  - Blood pressure using invasive technique.
  - Myocardial contractility
- **Electrolyte changes**
  - Na, and K level in plasma



- **Blood gases and acid base changes.**
- **Haematologic changes**
  - Size of RBCs
  - Hematocrit %
  - Survival time (after 4 hours) and survival rate.

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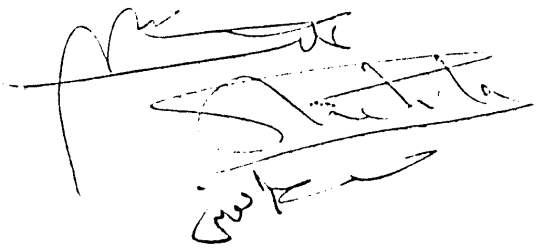

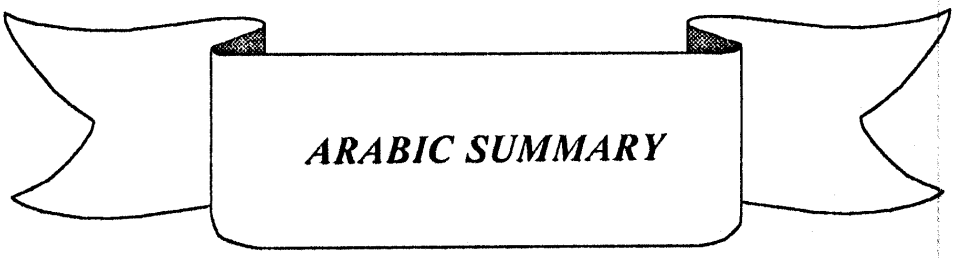
ARABIC SUMMARY

بسم الله الرحمن الرحيم

الملخـــــــص العربـــــــــى

بالرغم من التقدم الكبير فى اسلوب الإسعافات الأوليـة تعتبر الحـوادث وصدمة ما بعد النزف من أهم اسباب الوفاه والعجـز فـى سـن الشـباب• ومـن الحقائق المعروفة ان أهم العوامـل التـى تـؤدى الـى هبـوط فـى أجهـزة الجسـم المختلفة ومن ثم الى الوفاة بعد حدوث صدمة النزف هو إستمرار نقص تدفـق الدم داخل الشعيرات الدموية وبالتالى يؤدى الى نقص وصول كمية الأكسـجين اللازمة لحدوث العمليات الحيوية داخل الجسم•

وقد وجد ان الجهود المبذوله اثناء نقل المصاب عقب الإصابة مباشـرة انها تعمـل علـى خفـض عـدد الوفيـات بسـبب الحـوادث عـن طريـق التحديـث والتقدم فى أساليب الإنعاش من صدمة الـنزف ومنـع الهبـوط فـى ضغـط الـدم وفشل الدوره الدموية ومحاولة اعـادة معدل وصـول الأكسـجين الـى الإنسـجة للمعدل الكافى لإحتياجات الخلية•

أن الغرض من هذه الدراسة الوصول الى انسـب المحـاليل التـى يمكـن إستخدامها للتعويض المؤقت لفقد الدم فى حالات الحوادث للمحافظة على حيـاة المريض ومحاولة منع حدوث الوفاه او فشل فى اجهزة الجسم اثنـاء نقلـة الـى المستشفى واثناء الفترة اللازمه للإعداد لإجراء الجراحة اللازمه وتوفـير الـدم المناسـب الـلازم للمريـض وذلـك مـن خـلال مقارنـة فعاليـة المحـاليل متعادلـة التركيز و المحاليل عالية التركيز فى إنعاش صدمة ما بعد النزف•

ولقد تمت هذه الدراسة التجريبية على عدد ستون من الفئران البيضاء التى تزن ما بين ١٨٠ الى ٢٤٠ جم والمتوفره فى معامل كلية الطب البشرى بجامعة الزقازيق.

وقد تم تقسيم الفئران الى ٦ مجموعات متساوية كل مجموعة تتكون من ١٠ فئران.

وقد تم إحداث النزف من الفئران بعد تخديرها بنسبة ٣٠٪ من كمية الدم الموجوده داخل الجهاز الدورى لكل فأر عن طريق سحب الدم من الشريان السباتى المشترك بالرقبة.

ثم تم إسعاف الفئران بعد ٣٠ دقيقة من إحداث النزف بإستخدام احد المحاليل المختلفة المستخدمه فى هذه الدراسة وهى :

١- محلول لبنات الرنجر بمعدل ٦ مل لكل ١٠٠ جم من وزن الفأر .
٢- محلول كلوريد الصوديوم المركز (٧,٥٪) بمعدل ٠,٦ مل /١٠٠جم من وزن الفأر.
٣- محلول الدكستران ٧٠ بتركيز ٦٪ بمعدل ٠,٦ مل / ١٠٠ جم من وزن الفأر.
٤- محلول كلوريد الصوديوم ٧,٥٪ المضاف اليه الدكستران ٧٠ بتركيز ٦٪ ، معدل ٠,٦ مل / ١٠٠ جم من وزن الفأر.

ولقد تم قياس ضغط الدم وعدد نبضات القلب ومدلول معدل الإنقباض فى عضلة القلب قبل إحداث النزف وبعد الإنعاش بالمحاليل بخمس دقائق و ٣٠ دقيقة وساعة وساعتان وثلاث وأربع ساعات وكذلك تم قياس نسبة تركيز الصوديوم والبوتاسيوم بالدم ، ونسبة تركيز كرات الدم الحمراء ، وحجم كرات الدم الحمراء ونسبة غازات الدم قبل النزف وبعد الإنعاش بالحاليل بأربع ساعات.

ولقد كانت نتائج الدراسة بعد جمع البيانات وتحليلها احصائيا كالتالى :

أولا بالنسبة لديناميكية الدم :

كانت هناك زيادة ذات دلالة إحصائية فى نسبة إرتفاع ضغط الدم ، وعدد نبضات القلب ، ومدلول معدل إنقباض عضلة القلب بعد إستخدام جميع أنواع المحاليل كل على حده ولكن كانت الزيادة الإحصائية اكبر عند إستخدام المحاليل عالية التركيز (كلوريد الصوديوم ٧,٥٪ وحدة والمضاف اليه دكستران ٧٠) منه عند إستخدام المحلول متعادل التركيز وكذلك عند إستخدام محلول الدكستران (٧٠)٠

ثانيا بالنسبة لغازات الدم وقاعدية الدم :

أدى إستخدام المحاليل عالية التركيز الى زيادة احصائية فى قاعدية الدم اكبر منه فى حالة إستخدام المحاليل متعادلة التركيز ومحلول الدكستران ٧٠ وكذلك ادى الى تحسن ملحوظ فى نسبة ثانى اكسيد الكربون بالدم اكبر منه عند إستخدام المحاليل الأخرى٠

ثالثا : نسبة تركيز الصوديوم بالدم :

أدى أستخدام المحاليل عالية التركيز الى زيادة احصائية فى نسبة تركيز الصوديم بالدم فى حين ان المحاليل الأخرى لم تأثر فى نسبة تركيز الصوديم بالدم٠

رابعا : نسبة تركيز كرات الدم الحمراء بالدم :

أدى إستخدام المحاليل عالية التركيز الى نقص احصائيى ملحوظ فى نسبة تركيز كرات الدم الحمراء اكبر منه عند إستخدام المحاليل الأخرى٠

خامسا : بالنسبة لحجم كرات الدم الحمراء :

أدى إستخدام المحاليل عالية التركيز الى نقص إحصائيى معنوى فى حجم كرات الدم الحمراء فى حين ان إستعمال المحاليل الأخرى لم يؤثر فى حجم كرات الدم الحمراء٠

الخلاصـــــة

- أكدت هذه الدراسة ان المحاليل عالية التركيز (كلوريد الصوديوم ٧,٥٪ وكلوريد الصوديوم ٧,٥٪ المضاف اليه دكستران ٧٠ اكثر فاعلية فى إنعاش صدمة النزف ومنع الآثار الجانبية المترتبة عليه من المحاليل متعادلة التركيز (لبنات الرنجر) ومحلول الدكستران ٧٠ ٠

- إثبتت الدراسة ان محلول كلوريد الصوديوم المركز ٧,٥٪ وملحول كلوريد الصوديوم المركز ٧,٥٪ المضاف اليه دكستران ٧٠ متساويان فى الفاعلية عند إستخدام اى منهم فى إنعاش صدمة النزف٠

دور المحاليل عالية التركيز فى إنعاش صدمة النزيف لدى حيوانات التجارب

رسالة مقدمة من

الطبيب / وائل رشدى محمد يوسف

مدرس مساعد بقسم التخدير - طب الزقازيق

توطئة للحصول على درجة الدكتوراه

فى

"التخـــديـر"

تحت إشراف

الأستاذ الدكتور

محمد عزت مؤمن

أستاذ التخـــديـر

كلية الطب - جامعة الزقازيق

الأستاذ الدكتور

على عبد الرحمن سالم

أستاذ الفارماكولوجى

كلية الطب - جامعة الزقازيق

الدكتور

أسامة عبد الجواد نوفل

أستاذ مساعد التخدير

كلية الطب - جامعة الزقازيق

الدكتور

محمد شحتة توفيق

أستاذ مساعد التخدير

كلية الطب - جامعة الزقازيق

كلية الطب

جامعة الزقازيق

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